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(71) Applicant: LA JOLLA CANCER RESEARCH FOUNDATION [US/US]; 10901 North Torrey Pines Road, La Jolla, CA 92037 (US).

(72) Inventors: PASQUALE, Elena, B.; 6105 Dirac Street, San Diego, CA 92122 (US). SAJJADI, Fereydoun, G.; 1548 Plumtree Drive, Encinitas, CA 92024 (US).

(74) Agents: IMBRA, Richard, J. et al.; Campbell and Flores, Suite 700, 4370 La Jolla Village Drive, San Diego, CA 92122 (US).

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(57) Abstract

The invention provides substantially purified Eph-related protein tyrosine kinases, or functional fragments thereof, having about 23 to 66 percent amino acid sequence identity in their carboxyl terminal variable regions compared to known members of the Eph subclass of tyrosine kinases. Nucleic acids encoding such Eph-related protein tyrosine kinases, vectors and host cells are also provided. The invention also provides a method of diagnosing cancer and determining cancer prognosis. For example, the method provides for removing a tissue or cell sample from a subject suspected of having cancer and determining the level of Eph-related protein tyrosine kinase in the sample, wherein a change in the level or activity of an Eph-related protein tyrosine kinase compared to a normal sample indicates the presence of a cancer or indicates the level of malignancy of a cancer.

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NOVEL Eph-RELATED TYROSINE KINASES, NUCLEOTIDE SEQUENCES AND METHODS OF USE

This invention was funded in part by NIH Grants HD 26351 and CA 56721. Accordingly, the United States government has certain rights in the invention.

BACKGROUND OF THE INVENTION

This invention relates generally to protein tyrosine kinases and, more particularly, to Eph-related receptor tyrosine kinases and their manipulation for the control of cellular processes.

Receptor tyrosine kinases comprise a large family of proteins that share a number of structural features such as a glycosylated extracellular ligand-binding domain, a hydrophobic transmembrane domain and a conserved cytoplasmic catalytic domain. Integral membrane tyrosine kinases have been shown to mediate cellular signals important for growth and differentiation. The transduction of many extracellular signals to the cytoplasm occurs as a result of the binding of ligands such as growth factors, for example, to receptor tyrosine kinases at the cell surface. In most cases, ligand binding activates the cytoplasmic tyrosine kinase catalytic domain and culminates in tyrosine phosphorylation of multiple substrates in the cytoplasm.

Increased expression of membrane-spanning receptor tyrosine kinases frequently has been associated with alterations in normal cellular processes. The affected cellular processes include cell proliferation, differentiation and cancer, including, for example, human cancers. Specific examples of such cancers can include glioblastomas, squamous carcinomas and mammary carcinomas, which are associated with the amplification of the EGF receptor gene. Adenocarcinomas, breast cancers and gastric

cancers similarly are associated with aberrant expression of the HER2/neu receptor and certain breast carcinomas overexpress the erbB-3 gene, for example.

The correlation between aberrant expression and transforming ability also extends to members of the Eph subclass of receptor tyrosine kinases. For example, carcinomas of the liver, lung, breast and colon show elevated expression of Eph. Unlike many other tyrosine kinases, this elevated expression can occur in the absence of gene amplification or rearrangement. Such involvement of Eph in carcinogenesis also has been shown by the formation of foci of NIH 3T3 cells in soft agar and of tumors in nude mice following overexpression of Eph. Moreover, an antigen present on the surface of a pre-B cell leukemia cell line also has been identified as a member of the Eph subclass. Wicks et al., Proc. Natl. Acad. Sci., *USA* 89:1611-1615 (1992). This leukemia-specific marker, termed Hek, appears to be similar to the chicken Cek4 and mouse Mek4 of the Eph subclass of receptor tyrosine kinases (see Sajjadi et al., The New Biologist 3:769-778 (1991), which is incorporated herein by reference). As with Eph, Hek also was overexpressed in the absence of gene amplification or rearrangements in, for example, hemopoietic tumors and lymphoid tumor cell lines.

In addition to their roles in carcinogenesis, a number of transmembrane tyrosine kinases have been reported to play key roles during development. Examples include the mouse c-kit proto-oncogene and the *Drosophila* genes "sevenless" and "torso," which are involved in pattern formation. Consistent with this developmental role, many receptor tyrosine kinases other than those described above also have been shown to be developmentally regulated and predominantly expressed in embryonic tissues. Examples of these other tyrosine kinases include Cek1, which belongs to the FGF subclass, and the Cek4 and Cek5 tyrosine kinases

(Pasquale et al., Proc. Natl. Acad. Sci., *USA* 86:5449-5453 (1989); Sajjadi et al., *supra*, (1991); and Pasquale, E.B., Cell Reg. 2:523-534 (1991), all of which are incorporated herein by reference).

Eph was the first member of the Eph subclass of tyrosine kinases to be identified and characterized by molecular cloning (Hirai et al., Science 238:1717-1720 (1987)). The name Eph is derived from the name of the cell line from which the Eph cDNA was first isolated, the erythropoietin-producing human hepatocellular carcinoma cell line, ETL-1. The general structure of Eph is similar to that of other receptor tyrosine kinases and consists of an extracellular domain, a single membrane spanning region and a conserved tyrosine kinase catalytic domain. However, the structure of the extracellular domain of Eph, which comprises an immunoglobulin (Ig) domain at the amino terminus, followed by a cysteine-rich region and two fibronectin type III repeats in close proximity to the transmembrane domain, is completely distinct from that of previously described receptor tyrosine kinases. The juxtamembrane domain and carboxy-terminus regions of Eph also are unrelated to the corresponding regions of other tyrosine kinase receptors. Thus, the discovery of Eph defined a new subclass of receptor-type tyrosine kinases.

In addition to the isolation and characterization of Eph, other related tyrosine kinases now have been identified. Cek4 and Cek5 were identified by screening a chicken embryo cDNA expression library with anti-phosphotyrosine antibodies (Sajjadi et al., *supra*, (1991) and Pasquale, *supra*, (1991)). This method of identification was successful because Cek4 and Cek5 are expressed in embryonic tissues and have tyrosine kinase activity even when expressed as partial fragments in bacteria. Other Eph-related kinases that have been identified include Hek (Wicks et al., *supra*, (1992)), Sek

(Gilardi-Hebenstreit et al, Oncogene 7:2499-2506 (1992)), Eck (Lindberg and Hunter, Mol. Cell. Biol. 10:6316-6324 (1990)), Elk (Lhotak et al., Mol. Cell. Biol. 11:2496-2502 (1991)) and Eek (Chan and Watt, Oncogene 6:1057-1061 (1991)). These tyrosine kinases were cloned using a variety of methods.

The number of existing Eph-related kinases is not known and cannot be predicted. However, the Eph subclass already represents the largest known subclass of receptor tyrosine kinases, comprising at least 10 distinct members. The kinases belonging to the Eph subclass are so classified because each includes features such as the amino terminal Ig domain, the cysteine-rich stretch and two fibronectin type III repeats in the extracellular domain, which are conserved within the Eph subclass. However, despite these common structural features, the overall amino acid sequences outside the catalytic domain are quite different, indicating that different members of the Eph subclass interact with distinct ligands and substrates and, thus, exert distinct functions. This notion is supported by the differential distribution of different Eph-related kinases in adult tissues.

There is no indication whether other Eph-related kinases exist and, if so, what their relationship is to the known Eph-related kinases. Nevertheless, despite similarities among the Eph-related receptor tyrosine kinases, each is different and, as such, functions in related but distinct cellular processes. For example, many members of the Eph subclass are expressed in the nervous system during development and thus are likely to be involved in nerve regeneration processes. The aberrant expression or uncontrolled regulation of any one of these receptor tyrosine kinases can result in different malignancies and pathological disorders. Therefore, the identification and characterization of novel transmembrane

tyrosine kinases should provide important insights into the mechanisms underlying oncogenesis and cellular growth control pathways.

There thus exists a need to identify additional receptor tyrosine kinases and to manipulate them in order to diagnose pathological conditions and control cellular processes. The present invention satisfies this need and provides related advantages as well.

SUMMARY

The invention is directed to substantially purified Eph-related protein tyrosine kinases, or functional fragments thereof, having about 23 to 66 percent amino acid sequence identity in their carboxyl terminal variable region compared to the other known members of the Eph subclass of tyrosine kinases. Nucleic acids encoding such Eph-related protein tyrosine kinases, vectors and host cells also are provided. The invention also is directed to a method of diagnosing cancer. The method includes removing a tissue or cell sample from a subject suspected of having cancer and determining the level of Eph-related protein tyrosine kinase in the sample, wherein a change in the level or activity of a Eph-related protein tyrosine kinase compared to a normal sample indicates the presence of a cancer or correlates with a specific prognosis.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a comparison of the amino acid sequences from members of the Eph family. Dots replace residues in Cek4 (SEQ ID NO: 16), Cek6 (SEQ ID NO: 2), Cek7 (SEQ ID NO: 4), Cek8 (SEQ ID NO: 6), Cek9 (SEQ ID NO: 8), Cek10 (SEQ ID NO: 10), Eck and Eph that are identical to the corresponding residue in Cek5 (SEQ ID NO: 18). Dashes represent gaps introduced in the sequences to aid in the

alignment. The insertion sequence of Cek5 also is presented (Cek5*; SEQ ID NO: 12) and the insertion sequences of Cek7* (SEQ ID NO: 20) and Cek10* (SEQ ID NO: 14) are in parentheses. The conserved cysteines are indicated by the symbol " and the kinase domain is delimited by arrows. Open circles indicate the hydrophobic and aromatic residues that are conserved in the first fibronectin type III repeat and asterisks indicate the conserved residues of the second fibronectin type III repeat. The filled circle indicates the site of putative tyrosine autophosphorylation in the catalytic domain. The putative signal peptide sequences and transmembrane domains are underlined. Amino acids are numbered at the left of the sequences. The symbol + indicates the location of the extracellular domain amino acid insertion RICTPDVSGTVGSRPAADH (SEQ ID NO: 23), corresponding to Cek6 amino acids 426-444. Alignments were made by eye in the regions corresponding to Cek5 residues 1-615 and using the program DFALIGN (Feng and Doolittle, J. Mol. Evol., 25:351-360 (1987), which is incorporated herein by reference) in the regions corresponding to Cek5 residues 616-995.

Figure 2 shows a RNA blot analysis of Cek mRNAs. Polyadenylated chicken RNA from 10-day embryonic and adult tissues was hybridized with Cek-specific cDNA probes and with a chicken β-actin probe. Hybridization conditions were as described in Example I. The positions of RNA molecular weight standards (in kilobases, kb) are indicated on the right. β-actin transcripts are present in the ~2.0 kb size range.

Figure 3 shows a RNA blot analysis of Cek5 mRNAs. Polyadenylated RNA from body tissues (lanes 1 and 2) and brain (lanes 3 and 4) of 10-day chicken embryos was hybridized with a Cek5-specific cDNA (lanes 1 and 3). The same blots were then stripped and rehybridized with a 48 bp oligonucleotide antisense probe corresponding to the

juxtamembrane insertion sequence of Cek5 (lanes 2 and 4). Hybridization conditions were as described in Example I. The positions of RNA molecular weight standards (in kb) are indicated on the right.

Figure 4 shows immunoblotting with antibodies to different Eph-related kinases. Fractions from 10-day embryonic brain containing either membrane-associated proteins (M) or soluble proteins (S) were probed with anti-Cek4 (4), anti-Cek8 (8,) or anti-Cek9 (9) antibodies. Equal amounts of protein were loaded in all the lanes. IP, immunoprecipitates from 11-day embryonic retina with anti-Cek8 antibodies (8) or with normal rabbit IgGs (Ig). The immunoprecipitates were then probed with anti-Cek8 antibodies.

Figures 5.A. to 5.D. show the expression and tyrosine phosphorylation of Cek8 and Cek5 in transformed cell lines. Cell lysates were prepared from the rat central nervous system (CNS) tumor-derived cell lines B23, B28, B35, B49 and B50, the mouse embryonic carcinoma cell line, P19, and the human keratinocyte cell line HaCaT (Ha). Panels A and B show immunoprecipitates with anti-Cek8 antibodies. Panels C and D show immunoprecipitates with anti-Cek5 antibodies. The immunoprecipitation was followed by *in vitro* kinase reaction in the samples shown in panel C. The immunoblot in panel A was probed with anti-Cek8 antibodies. The immunoblots in panels B, C and D were probed with anti-phosphotyrosine antibodies.

Figures 6.A. to 6.F. demonstrate that Cek8 phosphorylation on tyrosine is increased in transformed cells and correlates with increased *in vitro* catalytic activity. Lysates from LMH cells and extracts of 10 day embryonic liver and adult liver were immunoprecipitated with anti-Cek8 antibodies, probed with anti-phosphotyrosine antibodies (panel A), then reprobed with anti-Cek8

antibodies (panel B). Lysates from normal chicken embryo fibroblasts and Rous sarcoma virus transformed chicken embryo fibroblasts were immunoprecipitated with anti-Cek8 antibodies, probed with anti-phosphotyrosine antibodies (panel C) and reprobed with anti-Cek8 antibodies (panel D).

Panels E and F show immunoblots of immunoprecipitated Cek8 (lane 1) or ß-galactosidase-Cek4 fusion protein substrate (lanes 2-5). The fusion protein was phosphorylated for 1 min at 37 °C by Cek8 (lane 2), 1 min at 37 °C by tyrosine phosphorylated Cek8 (lane 3), 1 min at 0 °C by Cek8 (lane 4), 1 min at 0 °C by tyrosine phosphorylated Cek8 (lane 5). Immunoblots were probed with anti-phosphotyrosine antibodies (panel E) and reprobed with anti-ß-galactosidase antibodies (panel F).

DETAILED DESCRIPTION OF THE INVENTION

The invention relates to the identification and characterization of seven novel members of the Eph subclass of membrane-spanning tyrosine kinases. The identification of these members doubles the number of kinases within this subclass, bringing the total to at least ten different Eph-related kinases. These Eph-related kinases therefore comprise the largest known subclass of integral membrane tyrosine kinases. The large number of different Eph-related kinases indicates that these receptors regulate a number of distinct cellular processes during development as well as in the adult organism. Therefore, identification of novel proteins within this subclass and isolation of their encoding nucleic acids allows the control of different cellular processes through the production of specific agonists and antagonists and through genetic therapy.

In one embodiment seven novel kinases of the Eph subclass of receptor protein tyrosine kinases have been

identified. The cDNAs encoding these Eph-related kinases were identified by hybridization at differential stringencies to identify distinct, but related receptor tyrosine kinases. All of the kinases exhibit gross structural features of known receptor tyrosine kinases in that they contain an extracellular ligand binding domain, a transmembrane domain and a cytoplasmic catalytic domain. These novel kinases are related to the Eph subclass of receptor tyrosine kinases and are designated Cek6 through Cek10$^+$ (SEQ ID NOS: 1 to 14, and 19 to 22.) The overall sequence identity between these Eph-related kinases varies significantly with each of the novel Eph-related receptors being identified by its carboxyl terminal variable region.

In another embodiment, the novel Eph-related kinases exhibit distinct tissue distribution patterns and developmental expression. Six of the kinases can be found to be expressed in both the embryonic brain and body tissues. The seventh Eph-related kinase, Cek5$^+$, is expressed only in the embryonic brain. Indicative of their roles in cellular processes, such as embryonic signal transduction pathways, these Eph-related kinases display distinct patterns of expression in adult tissues, including the neuronal specific expression of Cek5$^+$. These distinct patterns can be used to diagnose aberrations in normal cellular processes, such as those leading to uncontrolled malignant cell growth. For example, as described below, Cek8 activity is increased in various tumor cells as compared to normal cells. In addition to diagnosing such aberrations, it is also possible to treat defects caused by the unregulated expression of Eph-related kinases through the use of gene therapy. Reagents affecting the expression or activity of Eph-related kinases can also be useful for inducing nerve regeneration following injury.

As used herein, the term "Eph-related protein tyrosine kinase" or "Eph-related kinase" refers to a

receptor tyrosine kinase having an extracellular ligand binding domain, a transmembrane domain and a cytoplasmic catalytic domain, and belonging to the Eph subclass of receptor tyrosine kinases. Eph-related kinases include, for example, the receptor tyrosine kinases Cek6 (SEQ ID NO: 2), Cek7 (SEQ ID NO: 4), Cek7* (SEQ ID NO: 20), Cek7' (SEQ ID NO: 22), Cek8 (SEQ ID NO: 6), Cek9 (SEQ ID NO: 8), Cek10 (SEQ ID NO: 10), Cek5* (SEQ ID NO: 12) and Cek10* (SEQ ID NO: 14). Such kinases exhibit an overall amino acid sequence identity to Eph of greater than about 40 percent. The extreme carboxyl terminal cytoplasmic regions of the kinases are not well conserved and can be used to differentiate among them. This extreme carboxyl terminal cytoplasmic region begins just after the catalytic domain at about residue number 900 and extends to the C-terminal most residue. Therefore, the term "carboxyl terminal variable region" as used herein, refers to this extreme C-terminal region of the sequence which is divergent between the different members of the Eph subclass of tyrosine kinases. The actual sequence identities between different kinases within the Eph subclass are as follows: Cek5-Cek10: 66%; Cek5-Cek6: 54%; Cek5-Cek9: 50%; Cek5-Cek8: 38%; Cek5-Cek7: 34%; Cek5-Cek4: 24%; Cek5-Eek: 39%; Cek5-Eck: 36%; Cek5-Eph: 33%; Cek10-Cek6: 64%; Cek10-Cek9: 56%; Cek10-Cek8: 47%; Cek10-Cek7: 45%; Cek10-Cek4:32%; Cek10-Eek: 41%; Cek10-Eck: 39%; Cek10-Eph: 37%; Cek6-Cek9: 46%; Cek6-Cek8: 50%; Cek6-Cek7: 40%; Cek6-Cek4: 31%; Cek6-Eek: 39%; Cek6-Eck: 36%; Cek6-Eph: 32%; Cek9-Cek8: 46%; Cek9-Cek7: 47%; Cek9-Cek4: 29%; Cek9-Eek: 36%; Cek9-Eck: 33%; Cek9-Eph: 35%; Cek8-Cek7: 37%; Cek8-Cek4: 26%; Cek8-Eek: 39%; Cek8-Eck: 36%; Cek8-Eph: 30%; Cek7-Cek4: 36%; Cek7-Eek: 35%; Cek7-Eck: 43%; Cek7-Eph: 37%; Cek4-Eek: 29%; Cek4-Eck: 27%; Cek4-Eph: 23%; Eek-Eck: 26%; Eek-Eph: 32%; Eck-Eph: 52%. Therefore, the carboxyl terminal variable region exhibits an amino acid sequence identity of about 23 to 66 percent between the different Eph-related kinases. The novel Eph-related kinases described herein fall within

this level of sequence divergence and can therefore be distinguished by comparison to the known members of the Eph subclass. Known members of this subclass include, for example, Eph, Cek4, Cek5, Mek4, Hek, Sek (or mouse Cek8), Eck, Elk (or rat Cek6) and Eek.

It is understood that limited modifications may be made without destroying biological functions of Eph-related kinases and that only a portion of the entire primary structure may be required in order to effect a particular activity. Such biological functions and activities can include, for example, signal transduction, ligand binding and/or tyrosine kinase activity. For example, the Eph-related kinases of the invention have amino acid sequences substantially similar to those shown for Cek7, Cek7$^+$, Cek7$'$, Cek9, Cek10, Cek5$^+$, Cek10$^+$ and chicken Cek6 and Cek8 in Figure 1 (hereinafter referred to as Cek6 through Cek10$^+$), but minor modifications of these sequences which do not destroy their activity also fall within the definition of Eph-related kinases and within the definition of the protein claimed as such. Moreover, fragments of the sequences of Cek6 through Cek10$^+$ in Figure 1 (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 20 and 22), which retain the function of the entire protein as well as functional domains that contain at least one function of the intact protein are included within the definition. Functional domains can include, for example, active ligand binding and catalytic domains. The boundaries of such domains are not important so long as activity is maintained. It is also understood that minor modifications of the primary amino acid sequence can result in proteins which have substantially equivalent or enhanced function as compared to the sequences set forth in Figure 1 (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 20 and 22). These modifications may be deliberate, as through site-directed mutagenesis, or may be accidental such as through mutation in hosts which produce Eph-related kinases. All of these

modifications are included as long as biological function is retained. Further, various molecules can be attached to Eph-related kinases, for example, other proteins, carbohydrates, or lipids. Cek8 (SEQ ID NO: 6), for example, can contain complex N-linked oligosaccharides (see below). Such modifications are included within the definition of Eph-related tyrosine kinase.

The term "substantially purified," when used to describe the state of Eph-related tyrosine kinases denotes the protein free of a portion of the other proteins and molecules normally associated with or occurring with Eph-related kinases in their native environment. Such substantially purified Eph-related kinases can be derived from natural sources, recombinantly expressed or synthesized by *in vitro* methods so long as some portion of normally associated molecules is absent.

"Isolated" when used to describe the state of the nucleic acids encoding Eph-related tyrosine kinases denotes the nucleic acids free of at least a portion of the molecules associated with or occurring with Eph-related nucleic acids in the native environment.

As used herein, the term "vector" includes nucleic acids that are capable of harboring a natural or recombinant DNA sequence of interest. Vectors are usually derived from, or contain some sequences from, a natural source. For example, bacteriophage vectors containing specially engineered features that are largely derived from the phage's genome and are capable of carrying out some part of its infectious cycle. On the other hand, the sequences contained within plasmids are usually derived from different sources and compiled into a single molecule to carry out specific tasks. Thus, there are many different types of vectors and each is used according to the need to perform a desired function. Functions can include, for

example, propagation in a desired host, cloning recombinant or natural fragments of DNA, mutagenesis, expression and the like. In sum, "vector" is given a operative definition, and any DNA sequence which is capable of effecting a function of a specified DNA sequence disposed therein is included in this term as it is applied to the specified sequence.

The invention provides a substantially purified Eph-related protein tyrosine kinase, or functional fragment thereof. Also provided is a substantially purified chicken Eph-related protein tyrosine kinase. The substantially purified Eph-related protein tyrosine kinase exhibits about 23 to 66 percent amino acid sequence identity in its carboxyl terminal variable region compared to known members of the Eph subclass of tyrosine kinases. The amino acid sequences are substantially the same as that shown for Cek6 through Cek10* in Figure 1 (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 20 and 22.)

The invention also provides an isolated nucleic acid encoding a Eph-related protein tyrosine kinase, or functional fragment thereof. The isolated nucleic acid encoding a Eph-related protein tyrosine kinase exhibits about 23 to 66 percent amino acid sequence identity in its carboxyl terminal variable region compared to known members of the Eph subclass of tyrosine kinases. The encoding nucleotide sequences are substantially the same as that shown for Cek6 (SEQ ID NO: 1), Cek7 (SEQ ID NO: 3), Cek8 (SEQ ID NO: 5), Cek9 (SEQ ID NO: 7), Cek10 (SEQ ID NO: 9), Cek5* (SEQ ID NO: 11), Cek10* (SEQ ID NO: 13), Cek7* (SEQ ID NO: 19) and Cek7' (SEQ ID NO: 21) (hereinafter Cek6 through Cek10*).

The isolation of seven cDNAs that encode novel Eph-related receptor tyrosine kinases is disclosed herein. The predicted amino acid sequences of these Eph-related

kinases are shown in Figure 1 along with other known Cek kinase sequences and those of Eph and Eck. A number of conserved features serve to define the newly discovered kinases as members of the Eph subclass. These include an amino terminal immunoglobulin domain followed by a cysteine-rich stretch in the extracellular domain, with the position of most cysteines conserved, and sequences corresponding to two fibronectin type III repeats in close proximity to the transmembrane domain (O'Bryan et al., Mol. Cell. Biol. 11:5016-5031 (1991) and Pasquale, *supra*, (1991), the former of which is incorporated herein by reference). Potential sites of N-glycosylation are primarily localized in the C-terminal half of the extracellular regions. The homologies in the extracellular domains indicates that the different members of the Eph family can bind a similar class of ligands. Figure 1 also shows that the Eph family, with the inclusion of the new members that have been identified, can now be considered the largest known family of membrane-spanning tyrosine kinases. Such a large number of tyrosine kinases in this one class is surprising in view of the fact that the other families of receptor tyrosine kinases have fewer members.

The catalytic domains of the Eph-related kinases are highly conserved and exhibit amino acid identities ranging between 61% and 90%. The C-terminal tails are less conserved (Figure 1) and therefore constitute a variable region which can be used to specify the distinct Eph-related kinases. Only one of the tyrosines in the C-terminal variable region, corresponding to tyrosine 939 of Cek5, is conserved in all the members of the Eph family, with the exception of Cek4. This conserved tyrosine residue represents a likely site of autophosphorylation and regulation, Ullrich and Schlessinger, Cell 61:203-212 (1990). The large size of the Eph subclass of receptor tyrosine kinases, the variability within their sequences and their different tissue distributions indicate that each

receptor can, for example, serve distinct functions during cellular processes.

The variability in both the lengths and sequences of the juxtamembrane domains observed in the Eph-related kinases is unusual among tyrosine kinases belonging to the same subclass, Ullrich et al., *supra*, 1990. Because clones encoding variants with amino acid insertions in the juxtamembrane domain were isolated for Cek5, Cek7 and Cek10, the variability in the lengths of the juxtamembrane domains is likely to originate by alternative splicing (Figure 1). Juxtamembrane domains are important for the modulation of receptor functions by heterologous stimuli, for example, through phosphorylation by other kinases. The juxtamembrane domains of the members of the Eph family contain numerous serines, threonines and tyrosines that can serve as sites of regulation by phosphorylation, Kemp et al., Trends Biol. Sci. 15:342-346 (1990), which is incorporated herein by reference. For example, Cek9 and Cek10, as well as Cek5, Cek6, and Eck contain the consensus sequence (S/T)P, which is recognized by proline-dependent protein kinases such as cdc2, Kemp et al., *supra*, (1990). Juxtamembrane domains have also been indicated to be important in the regulation of the subcellular distribution of the kinase and in the binding of some substrates (Ullrich et al., *supra*, 1990).

The mRNA corresponding to Cek5* (SEQ ID NO: 11), the variant form of Cek5, was shown to be specifically expressed in the CNS, indicating that Cek5* functions primarily in neuronal cellular functions. Indicative of this is another tyrosine kinase, src, which has been shown to encode neuronal specific variants containing 6 to 17 amino acid insertions in the regulatory (non-catalytic) region (Brugge et al., Nature 316:554-557 (1985); Martinez et al., Science 237:411-415 (1987); Pyper et al., Mol. Cell. Biol. 10:2035-2040 (1990), all of which are

incorporated herein by reference). These neuronal forms of c-src have higher specific catalytic activity than non-neuronal c-src.

Although the predicted molecular masses of the different members of the Eph family are similar, the sizes of their transcripts appear quite varied (4 to 10 kb). In addition, several mRNA species for each of the Eph-related kinases, particularly in the CNS, were detected using a panel of probes. As described below, the patterns of expression of these novel Eph-related kinases are also distinct.

DNA sequences encoding the polypeptides of Eph-related kinases can be obtained by methods known to one skilled in the art. The sequences described herein are sufficient for one skilled in the art to practice the invention. Such methods include, for example, cDNA synthesis and polymerase chain reaction (PCR). The need will determine which method or combination of methods is to be used to obtain the desired sequence. Expression can be performed in any compatible vector/host system. Such systems include, for example, plasmids or phagemids in procaryotes such as *E. coli*, yeast systems and other eucaryotic systems such as mammalian cells. Additionally, the Eph-related kinases can also be expressed in soluble or secreted form depending on the need and the vector/host system employed.

Such vectors and vector/host systems are known, or can be constructed by those skilled in the art and should contain all expression elements necessary for the transcription, translation, regulation, and sorting of the polypeptide which makes up the Eph-related kinase. Other beneficial characteristics may also be contained within the vectors such as mechanisms for recovery of the nucleic acids in a different form. Phagemids are a specific

example of this because they can be used either as plasmids or as bacteriophage vectors. The vectors can also be for use in either procaryotic or eucaryotic host systems so long as the expression elements are of a compatible origin. One of ordinary skill in the art will know which host systems are compatible with a particular vector. Thus, the invention provides vectors, host cells transformed with the vectors and Eph-related kinases produced from the host cells containing a nucleic acid encoding a Eph-related kinase.

The invention also provides methods of diagnosing cancer and determining cancer prognosis. The method includes removing a tissue or cell sample from a subject suspected of having cancer and determining the level of Eph-related protein tyrosine kinase in said sample, wherein a change in the level or activity of a Eph-related protein tyrosine kinase compared to a normal sample indicates the presence of a cancer or indicates the level of malignancy of a cancer and, therefore, the most appropriate course of treatment.

As stated previously, receptor tyrosine kinases are involved in many signal transduction events that regulate important cellular processes. Such processes include, for example, cellular differentiation and proliferation. Abnormal regulation or expression of the signal transduction machinery can lead to aberrant and malignant growth of the abnormally regulated cells. Abnormal expression of Eph is known to be associated with carcinomas of the liver, lung, breast and colon, for example. Likewise, since some Eph-related tyrosine kinases are, at least, found within the same tissues as Eph, their abnormal expression may also lead to the development of the carcinomas described above as well as other types of cancers. For example, increased Cek8 activity was found in embryonal carcinoma cells and a keratinocyte tumor cell

line (see Example II). Additionally, cancers of the neuronal linage are likely to be caused by the abnormal expression or regulation of an Eph-related kinase such as Cek8 (see Example II) or Cek5* since this Eph-related kinase is found exclusively in neuronal tissues. Cek5*, Cek5 and the other Eph-related kinases expressed in the nervous system also are likely to be involved in nerve regeneration.

The important role that these receptor tyrosine kinases play in cellular processes can be advantageously used to diagnose early stages of cancer within a cell sample or tissue. A change in the amount or activity of an Eph-related kinase in a suspected sample, compared to a normal sample, will be indicative of cancerous stages and of their level of malignancy. Depending on whether the normal state is caused by the presence or absence of an Eph-related kinase, the change can involve either an increase or decrease in the amount or activity of the Eph-related kinase. For example, Cek8 activity is increased in various tumor cells (see Example II). Thus, increased activity of an Eph-related kinase of the invention such as Cek8 (SEQ ID NO: 6) can be useful for identifying the presence of transformed cells such as occur in a cancer.

One skilled in the art can measure the level or activity of an Eph-related kinase, for example, in a tissue sample obtained from a subject suspected of having a cancer or a developmental abnormality and the level or activity of the Eph-related kinase can be compared to the level or activity known to be present in a normal sample. Such a known level of activity can be determined by obtaining a significant number of tissue samples from subjects that do not have a cancer or a developmental abnormality and measuring the levels or activities of an Eph-related kinase in the population of samples. Methods for determining the level or activity of Eph-related kinases are known to the

skilled artisan and include, for example, RNA and protein blot analysis, ELISA using specific antibodies to each of the Eph-related kinases and direct measurement of catalytic activity such as tyrosine kinase activity. Such methods are described in detail in Example II or are otherwise known in the art (see, for example, Harlow et al., Antibodies: A Laboratory Manual Cold Spring Harbor Laboratory (1988), which is incorporated herein by reference).

The following examples are intended to illustrate, but not limit the invention.

EXAMPLE I

Isolation and Characterization of Eph-Related Tyrosine Kinases

This example shows the cloning and sequencing of the Eph-related kinases Cek6 through Cek10*. Structural characteristics and patterns of expression are also described.

To find novel members of the Eph family, various cDNA probes were used at different stringencies to screen a 10 day embryonic library as well as a 13 day embryonic brain cDNA library. The probes were derived from Cek4 (SEQ ID NO: 15) or Cek5 (SEQ ID NO: 17), which had been previously isolated based on phosphotyrosine content. Following subcloning and sequence analysis, it was found that the newly isolated cDNA clones encoded seven different Eph-related tyrosine kinases. Their isolation and structure are described below.

Briefly, a 10-day chicken embryo λgt11 cDNA library (Clontech) and a 13-day embryonic brain λgt11 cDNA library were used to isolate the cDNA clones. Screening was performed at different stringencies using the following procedure. Plaques were transferred to nylon membranes

(Micron Separations Inc.) on duplicate filters and hybridized to the appropriate probes at one of two stringencies (50% formamide, 42°C; or 50% formamide, 37°C). Conditions used were those recommended by the manufacturer and probes were detected using a nonradioactive DNA labeling and detection method (Boehringer Mannheim). Plaques identified as positive were subjected to three rounds of purification prior to DNA extraction using Lambda-TRAP (Clontech). Inserts from recombinant lambda DNA were subcloned in pBluescript vectors (Stratagene, San Diego, CA) using standard procedures and the sequences were analyzed on both strands, using the dideoxynucleotide chain-termination technique with Sequenase (United States Biochemical, Cleveland, OH).

Several clones distinguishable over known Eph tyrosine kinases were isolated using the Cek5 probe, which corresponded to nucleotides 495-3223 (Pasquale, *supra*, (1991)). The clones include: one Cek5$^+$ cDNA clone (from the chick embryo library); three Cek6 clones (two from the embryonic brain and one from the chick embryo library); one Cek7 clone (from the chick embryo library); one Cek7$^+$ clone (from the chick embryo library); one Cek7$^-$ clone (from the embryonic brain library); one Cek9 clone (from the chick embryo library); one Cek10$^+$ clone (from the chick embryo library) and two Cek10 or Cek10$^+$ clones, which are indistinguishable because they do not encode the juxtamembrane domain, (one from the chick embryo and one from the embryonic brain library).

A Cek4 probe (corresponding to nucleotides 748-1756; see Sajjadi et al., *supra*, 1991), on the other hand, was used to isolate one Cek8 clone (from the chick embryo library). Also, following its initial isolation, a Cek10 probe, corresponding to residues 400-596 in Figure 2, was used to isolate clones extending further into the 5$^-$ end

from the chick embryo library. Of the two clones isolated, one represented Cek10 and one Cek10$^+$.

The above-identified Eph-related kinases were characterized in terms of tissue distribution and expression by RNA blot analysis. Poly-A$^+$ RNA was prepared from chicken tissues using the procedure of Badley et al., Biotechniques 6:114-116 (1988), which is incorporated herein by reference. Poly-A$^+$ RNA (4-5 μg) was size-fractionated alongside RNA molecular weight markers on 0.9% agarose gels containing formaldehyde (Sambrook et al., Molecular Cloning: A Laboratory Manual (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989), which is incorporated herein be reference) and transferred to nitrocellulose filters (Schleicher & Schuell) according to methods known to one skilled in the art. The membranes were prehybridized for 2 hours and then hybridized under stringent conditions (50% formamide, 5x SSPE, 5x Denhardt's reagent, 0.5% SDS, 100 μg/ml salmon testes DNA, 42°C). Probes were labeled with ^{32}P dATP by the random-primed method of Feinberg and Vogelstein, Anal. Biochem. 132:6-13 (1983), which is incorporated herein by reference. T4 polynucleotide kinase was used to label the 5' end of the Cek5$^+$ specific oligonucleotide (Sambrook et al., *supra*, 1989). Filters were washed to a final stringency of 0.1x SSPE, 0.1% SDS at 58°C prior to exposure to Kodak XAR-5 X-ray film. For autoradiography of β-actin controls, intensifying screens were typically omitted and exposure time was reduced to 2 hours.

The following cDNA probes were used for RNA blot analysis: Cek4, 1.2 kb, same probe used for the library screening described previously, hybridizes to the region encoding amino acid residues 240-575; Cek5 probe, 1.2 kb, hybridizes to the 3' untranslated region; Cek6 5' probe, 1.3 kb, hybridizes to amino acid residues 1-438; Cek6 3' probe, 0.6 kb, hybridizes to the region following amino

acid 844; Cek7 5' probe, 0.4 kb, hybridizes to amino acid residues 1-136; Cek7 3' probe, 2.0 kb, hybridizes to the region following amino acid 137, including the 3' untranslated region; Cek8 probe, 1.2 kb, hybridizes to the region encoding amino acid residues 1-406; Cek9 probe, 0.6 kb, hybridizes to the region encoding amino acid residues 1-208; Cek10 probe, 0.6 kb, hybridizes to the region encoding the 10 C-terminal amino acids and to about 600 nucleotides of 3' untranslated region. For Cek6 and Cek7, the 3' Cek6 probe and the 5' Cek7 probe were used for the embryonic tissues mRNAs and a mixture of 5' and 3' probes for the adult tissues mRNAs.

Polyadenylated RNA was isolated from a number of adult chick tissues, as well as from brain and body tissues of 10-day embryos. These RNAs were then used for RNA blot analysis using the above specific probes. Probes were designed to minimize the possibility of cross-hybridization among the related kinases. Chicken β-actin DNA was used as a control probe (Cleveland et al., Cell 20:95-105 (1980), which is incorporated herein by reference).

The amino acid sequence of Cek4 (SEQ ID NO: 16) is 67% identical to that of Cek5 (SEQ ID NO: 18) in the catalytic and C-terminal regions and is most closely related to that of Cek7 (SEQ ID NO: 4) (75% amino acid identity in the same regions) (Figure 1). Preliminary data had indicated that Cek4 was highly expressed in the chicken developing brain and embryonic tissues, but no information was obtained on the adult pattern of expression in the chick. These data were therefore included in Figure 2. The 7.5 kb Cek4 transcript previously described was confirmed to be abundant in 10 day embryonic tissues. Expression was pronounced in the adult brain and retina, and lower but detectable in all other adult tissues examined, except the liver. In addition to the major 7.5 kb transcript, a smaller Cek4 transcript (of about 5 kb)

was found to be expressed at lower levels in the adult brain.

The Cek6 amino acid sequence (SEQ ID NO: 2) is most closely related to that of rat Elk (96% identity in the catalytic and C-terminal regions). Of the Cek members of the Eph subclass, Cek6 is most closely related to Cek5 (SEQ ID NO: 18) and Cek10 (SEQ ID NO: 10) (82% amino acid identity with both, in the catalytic and C-terminal regions) (Figure 1). The two Cek6 cDNAs that were isolated from a 13-day chick embryo brain library were identical and both encoded a protein with a deletion of 32 amino acids and an insertion of 19 amino acids in the extracellular region (Figure 1). However, these may be cloning artifacts, particularly the deletion, since it causes a shift in the reading frame and the premature termination of the encoded protein. A 4.4 kb Cek6 transcript was found to be expressed at high levels in the 10-days embryo and in adult brain, lung, heart and skeletal muscle (Figure 2). Low levels of Cek6 expression were detected in all other adult tissues tested. A second larger Cek6 transcript of about 6.5 kb was detected at low levels in the adult brain.

The amino acid sequence of Cek7 (SEQ ID NO: 4) is 71% identical to that of Cek5 (SEQ ID NO: 18) in the catalytic and C-terminal regions and is most closely related to those of Cek4 (SEQ ID NO: 16) and Cek9 (SEQ ID NO: 8) (75% amino acid identity with both, in the same regions) (Figure 1). A variant form of Cek7, containing a 22 amino acid insertion in the juxtamembrane domain (Figure 1) also was isolated and designated Cek7*. Cek7 (SEQ ID NO: 4) and Cek7* (SEQ ID NO: 20) may originate from the same gene by alternative splicing. A second variant form of Cek7, designated Cek7' (SEQ ID NO: 22), which also presumably originates via alternative splicing, differs from Cek7 in the C-terminal 33 amino acids. Cek7 appears to have the lowest levels of expression among all the Eph

related kinases examined. Three different transcripts of about 4.4 kb, 7 kb and 8.5 kb were detected in the 10-day embryonic brain. Expression was weaker in the rest of the 10-day embryo, where only the 4.4 kb transcript could be detected (Figure 2). Cek7 transcripts were not detected in the adult tissues, except for a barely detectable 8.5 kb transcript in the brain (Figure 2).

Cek8 (SEQ ID NO: 6) is equally related to Cek5 (SEQ ID NO: 18), Cek6 (SEQ ID NO: 2), Cek7 (SEQ ID NO: 4) and Cek10 (SEQ ID NO: 10) (74% amino acid identity in the catalytic and C-terminal regions) (Figure 1). A single 6 kb Cek8 transcript was found to be present in both the 10-day embryonic brain and body tissues (Figure 2). Cek8 (SEQ ID NO: 6) expression appears to be the highest in adult brain and retina and is also detectable in kidney, lung, skeletal muscle and thymus (Figure 2; see, also, Example II). Cek8 expression was not detected in heart and liver.

Cek9 (SEQ ID NO: 8) is most closely related to Cek5 (SEQ ID NO: 18) (77% identity at the amino acid level in the catalytic and C-terminal regions (Figure 1). A 4.4 kb Cek9 transcript is present in embryonic brain and body tissues. Two additional and very minor transcripts of about 5.5 kb and 6.5 kb were detected exclusively in the 10-day embryonic brain (Figure 2). Among the adult tissues examined, Cek9 expression is prominent in the thymus and detectable in brain, retina, kidney, lung and heart. None of the other kinases examined displays such an elevated level of expression in the thymus. Cek9 expression was not detected in skeletal muscle and liver.

Cek10 (SEQ ID NO: 10) is most closely related to Cek5 (SEQ ID NO: 18) and Cek6 (SEQ ID NO: 2) (84% amino acid identity with both in the catalytic and C-terminal regions) (Figure 1). A variant form of Cek10, containing a 15 amino acid insertion in the juxtamembrane domain

(Figure 1), was also isolated and designated Cek10$^+$ (SEQ ID NO: 14). Cek10 and Cek10$^+$ may originate from the same gene by alternative splicing. Northern blot analysis identified two Cek10 transcripts of about 4.4 kb and 6 kb, present at different relative levels in 10-day embryonic brain and body tissues as well as in a number of adult tissues (Figure 2). Among the adult tissues examined, Cek10 expression was particularly prominent in the kidney. Lower Cek10 expression was detected in the lung and barely detectable transcripts were also present in brain, liver, heart, skeletal muscle and thymus.

A variant form of Cek5, containing a 16 amino acid insertion in the juxtamembrane domain, was also identified and termed Cek5$^+$ (SEQ ID NO: 12) (Figure 1). This Cek5 variant may originate as a result of alternative splicing. With a Cek5 DNA probe recognizing both Cek5 and Cek5$^+$ (see Material and Methods), a 4.4 kb transcript was detected in both 10-day embryonic brain and body tissues (Figure 3, lanes 1 and 3). In addition, a much larger transcript (of about 10 kb) was detected in the 10-day embryonic brain (Figure 3, lane 3). Consistently with the previously reported expression of the Cek5 protein, Cek5 transcripts are more abundant in the brain than in other 10-day embryonic tissues. Using a probe corresponding to the 16 amino insertion in the juxtamembrane domain (Figure 3, lanes 2 and 4), Cek5$^+$ was found to be exclusively expressed in the CNS and only as the 4.4 kb transcript. Because Cek5 immunoreactivity in the CNS has been previously found to be confined to neurons, Cek5$^+$ appears to be a neuronal specific variant of Cek5.

Polyclonal antibodies recognizing specifically Cek4, Cek8 and Cek9 have been obtained and will be used for the characterization of these kinases (see Example II). Peptides corresponding to the carboxy-terminal ends of Cek4, Cek8 and Cek9 were coupled to bovine serum albumin

(BSA) with m-maleimido benzoyl-N-hydroxysuccinimide ester (Cek4) or with glutaraldehyde (Cek8 and Cek9) and used as immunogens. The peptides used were the following: Cek4, CLETHTKNSPVPV (SEQ ID NO 24); Cek8, KMQQMHGRMVPV (SEQ ID NO 25) and Cek9, KVHLNQLEPVEV (SEQ ID NO 26). The carboxy-terminal regions were chosen because they are poorly conserved within the Eph subclass, increasing the likelihood of obtaining antibodies specific for each kinase.

The antibodies were purified from the antiserum by affinity-chromatography on the appropriate peptides coupled to N-hydroxy-succinimide-activated agarose (BioRad). As shown in Figure 4, after affinity purification the antibodies to Cek4, Cek8 and Cek9 recognize a single band of the expected apparent molecular mass (about 120 kiloDalton, kDa) in membranes-containing fractions isolated from 10-day embryonic brain, but not in fractions containing soluble proteins. These antibodies do not cross-react significantly with related members of the Eph subclass (not shown) and can be used for different applications such as immunoblotting, immunofluorescence microscopy and immunoprecipitation (see Figure 4). All of the antibodies are capable of immunoprecipitating the kinases from tissue extracts and, as expected, the immunoprecipitated kinases undergo *in vitro* autophosphorylation in the presence of ATP (see Example II).

These techniques will allow the characterization of the kinases of the Eph subclass at the protein level. Coupled to a solid support, the antibodies can also be used to purify the kinases from tissues and cell lines. In the cases tested, antibodies generated to the chicken Eph-related kinases recognize the corresponding mammalian homologues. Thus, these antibodies could be used, for

example, to screen tumor samples for the presence of the appropriate Eph-related kinases.

EXAMPLE II

CHARACTERIZATION OF CEK8

This example describes structural and functional characteristics of the Cek8 protein (SEQ ID NO: 6), including the expression and activity of Cek8 during development and in tumor cells.

A. Antibody preparation:

Cek8 expression and activity was examined using immunological and immunohistochemical methods. An antigen for raising anti-Cek8 antibodies was prepared by coupling the peptide KMQQMHGRMVPV (SEQ ID NO: 25), which consists of the eleven carboxy terminal amino acids of Cek8, including an additional N-terminal lysine, to BSA using glutaraldehyde (Harlow and Lane, *supra*, 1988). An antigen for raising anti-Cek4 antibodies was prepared by coupling the peptide CLETHTKNSPVPV (SEQ ID NO: 24), which corresponds to the 12 carboxy terminal amino acids of Cek4, including an additional cysteine at the N-terminus, to BSA using m-maleimidobenzoyl-*N*-hydroxysuccininmide ester (Harlow and Lane, *supra*, 1988). Anti-Cek5 antibodies and anti-phosphotyrosine antibodies were prepared as described by Pasquale, *supra*, (1991). Antisera were raised in rabbits using standard methods (see, for example, Harlow and Lane, *supra*, 1988). The peptide antigen was coupled to N-hydroxy-succinimide-activated agarose and specific antisera were affinity purified.

B. Structural characterization of Cek8:

Cek8 was immunoprecipitated and examined by immunoblotting as described in Section C.1., below. The

affinity purified anti-Cek8 antibodies recognized a protein having an apparent molecular mass of about 120 kDa, which was the expected size for Cek8. The calculated molecular mass of Cek8, however, is less than the 120 kDa observed by SDS-PAGE. Since Cek8 contains three consensus sites of *N*-linked glycosylation, Cek8 was examined for such glycosylation. When chicken embryo fibroblasts were grown in the presence of 1.6 μg/ml tunicamycin, which inhibits *N*-linked glycosylation, the apparent molecular mass of Cek8 decreased by about 10 kDa.

In order to characterize the carbohydrate moiety of Cek8, lectin affinity chromatography was performed. Ten day embryonic chicken brains were sonicated in 10 ml PBS containing protease inhibitors (protease inhibitors are 1 mM phenylmethylsulfonyl fluoride, 0.2 trypsin inhibitor units aprotinin/ml, 10 μg/ml pepstatin and 10 μg/ml leupeptin and 1 mM sodium orthovanadate, a phosphatase inhibitor. The sonicated material was centrifuged at 2000 x g for 5 min to remove insoluble material, then the supernatant was centrifuged at 200,000 x g for 40 min.

The pellet, which contained the membrane enriched fraction, was solubilized in PBS containing 0.1% Triton X-100. The solubilized sample was centrifuged 5 min in a microfuge and the supernatant was collected. The extract was dialyzed overnight at 4 °C against 10 mM Tris-HCl, pH 7.4, loaded onto various lectin columns, including concanavalin A, lentil lectin, wheat germ agglutinin, ricin I lectin, peanut lectin or *Ulex europaeus* I lectin (EY Laboratories, Inc.; San Mateo CA), and the columns were eluted with 0.1 M methyl α-D-mannopyranoside, 0.1 M D-mannose, 0.1 M N-acetyl-D-glucosamine, 0.1 M α-lactose, 0.1 M α-lactose or 0.05 M α-L-fucose, respectively. Fractions were collected and analyzed by immunoblotting for the presence of Cek8 as described below.

Cek8 bound to the concanavalin A, lentil lectin, ricin I and wheat germ agglutinin columns and was eluted with the appropriate buffers. These lectins preferentially recognize *N*-linked sugar chains. Thus, this result is in agreement with the observed inhibition of glycosylation by tunicamycin. In contrast, Cek8 does not bind to peanut lectin, which primarily recognizes *O*-linked chains.

Binding to concanavalin A and elution with the relatively low concentration of 0.1 M methyl α-D-mannopyranoside indicates that Cek8 contains biantennary complex type sugar chains (Osawa and Tsuji, Ann. Rev. Biochem. 56:21-42 (1987)). Binding to lentil lectin indicates that a fucose residue is present on the innermost *N*-acetylglucosamine residue in an oligosaccharide core. However, since Cek8 does not bind with *Ulex europaeus* I lectin, terminal fucose residues are not likely present (Sugii and Kabat, Carb. Res. 99:99-101 (1982)). Binding of Cek8 to wheat germ agglutinin indicates that sialic acid is present and binding to the ricin I column indicates that terminal ß-galactosyl residues are present in complex sugar chains. These carbohydrate structures likely are located in the extracellular regions of Cek8 and can participate in interactions with extracellular molecules. *In vivo* phosphorylation on tyrosine of Cek8 can be achieved by exposing cells expressing Cek8 to wheat germ agglutinin.

C. Expression and Catalytic Activity of Cek8:

This section describes the methods for determining Cek8 expression and activity in various tissues during development and in tumor cells.

1. Methods

Cek8 expression and activity were determined by immunoprecipitation and immunoblot experiments. Cells from

90% confluent tissue culture plates were washed 3x with ice cold phosphate buffered saline (PBS), collected in cold RIPA buffer (150 mM sodium chloride, 10 mM sodium phosphate, pH 7.2, 1% deoxycholate, 1% Triton X-100, 0.1% SDS) containing protease inhibitors, and lysed by sonication. Phosphotyrosine was added to a final concentration of 8 mM when immunoblotting was performed using anti-phosphotyrosine antibodies.

Tissues were removed from adult chickens or chicken embryos and sonicated in PBS containing protease inhibitors. Whole embryos were collected and sonicated in PBS. Lysates were stored at -70 °C. Protein concentrations were determined using a Bio-Rad protein assay (Bio-Rad Laboratories; Richmond CA). For immunoprecipitations, tissue extracts were diluted in RIPA buffer. Cell lysates and tissue extracts in RIPA buffer were precleared using Staph A (Boehringer-Mannheim; Indianapolis IN) as described by Pasquale (*supra*. 1991). The samples then were incubated 40 min with 20 μg anti-Cek4, anti-Cek5 or anti-Cek8 antibodies or 20 μg control rabbit IgG preabsorbed to 20 μl Staph A. The amount of antibody was selected to ensure that all of the antigen in the extracts or lysates was precipitated.

Immunoprecipitated material was washed 3x with RIPA buffer and 1x with PBS. Sample buffer was added, the immunoprecipitates were boiled for 5 min, separated by SDS-PAGE on 7.5% gels and transferred to nitrocellulose as described by Towbin et al., Proc. Natl. Acad. Sci., *USA* 76:4350-4354 (1979), which is incorporated herein by reference. Following transfer, the filters were incubated overnight in Tris-hydroxyethylaminoethane-buffered saline (TBS) containing 3% BSA, then incubated 4 hr in 3% BSA containing 3 μg/ml anti-Cek4, anti-Cek5, anti-Cek8 or anti-phosphotyrosine antibody. The filters were rinsed with TBS, then incubated for 1 hr with 0.2 μg/ml protein A

peroxidase (Sigma; St. Louis MO) in TBS containing 3% BSA. The filters were rinsed several times with TBS and developed using enhanced chemiluminescence reagents (Amersham; Arlington Heights IL). In some experiments, after detection, the filters were dried for a few hours, then incubated in 3% BSA in TBS and probed with a different antibody.

In vitro phosphorylation was performed as described by Pasquale, *supra*, (1991). Briefly, Cek8 was immunoprecipitated from 10 day embryonic brain extracts or from cell lysates. In control experiments, Cek5 was immunoprecipitated. Immunoprecipitations were performed as described above. The immune complexes were incubated for 30 min at 37 °C in phosphorylation buffer (25 mM N-2-hydroxyethylpiperazine-N '-2-ethanesulfonic acid, pH 7.5, 10 mM $MgCl_2$, 10 mM $MnCl_2$, 1 mM sodium orthovanadate, 0.1% Triton X-100, 150 μM ATP). Sample buffer was added and electrophoresis and transfer to nitrocellulose were performed as described above. Following transfer, the filters were incubated overnight in 3% BSA in TBS, then incubated 4 hr in 3% BSA containing 3 μg/ml anti-phosphotyrosine antibodies.

2. Cek8 expression and activity during development

In whole embryo extracts, Cek8 expression was detectable at embryonic day 3, increased gradually between embryonic days 3 and 5, then remained relatively constant through embryonic day 10, which was the last timepoint examined. Cek8 was phosphorylated on tyrosine *in vivo* at a low level in 10 day embryonic brain. In addition, Cek8 underwent autophosphorylation on tyrosine *in vitro* in the presence of ATP and divalent metal ions.

Cek8 expression also was examined in various tissues of 10 day chicken embryos. Cek8 was most abundant

in the brain and retina, was expressed at substantial levels in thigh, gizzard and lungs and at lower levels in intestine, liver, lens and heart. Cek8 was not detectable in blood.

The developmental regulation of Cek8 expression was examined in greater detail in cerebrum, cerebellum, retina and thigh. In the cerebrum, Cek8 expression is low at embryonic day 6, then gradually increases to a maximal level at embryonic days 16 to 20. Cek8 expression is low, but detectable, in adult cerebrum. In contrast, expression in the cerebellum is low at embryonic day 12 and barely detectable at later stages of development. In thigh muscle, Cek8 expression is highest at embryonic day 7, then decreases to barely detectable levels by day 13, before terminal skeletal muscle differentiation occurs. In the retina, Cek8 expression remains relatively constant from embryonic day 8 until hatching.

Cek 8 expression also was examined by immunoperoxidase staining in chicken embryo frozen tissue sections. Embryos were removed from eggs, fixed in 4% formaldehyde, 0.1 mM sodium orthovanadate in PBS for 16 to 24 hr, then cryoprotected in 20% sucrose in PBS, 0.1 mM sodium orthovanadate for 24 hr. Embryos were embedded in OCT compound (Miles Inc.; Tarrytown NY), then frozen in dry ice/2-methylbutane. Ten μm cryostat sections were collected on glass slides and stored at -70 °C.

The sections were treated with 0.3% hydrogen peroxide for 10 min, then blocked with 3% BSA or normal goat or horse serum in PBS for 30 min. Sections were incubated with rabbit anti-Cek8 antibodies (10-20 μg/ml) or mouse anti-200 kDa neurofilament protein antibodies (1 μg/ml; Boehringer Mannheim; Indianapolis IN) in a 1:50 dilution of normal goat serum or horse serum for 30 min.

Controls were performed using anti-Cek8 antibodies that were preincubated with the antigen.

Following incubation with the primary antibody, the sections were rinsed with PBS and incubated with biotinylated goat anti-rabbit or horse anti-mouse IgG (Vector Labs; Burlingame CA). After additional washes with PBS, the sections were incubated with an avidin-biotin-peroxidase complex or with an avidin-biotin-alkaline phosphatase complex (Vector Labs). Following several washes in PBS, peroxidase or alkaline phosphatase were visualized using the appropriate substrate kit (Vector Labs). The sections then were rinsed in PBS, air dried, mounted in Permount and sealed with a #1 coverslip. Specimens were photographed with a Zeiss 405M inverted microscope.

Cek8 immunoreactivity was intense in the spinal cord and the spinal nerves. Localization of Cek8 in the spinal nerves was similar to that of a 200 kDa neurofilament protein. At embryonic day 6, Cek8 expression was restricted to the ventral portions of the spinal nerves, which contain axons of motor neurons.

The results of these experiments indicate that Cek8 is expressed early in development. In general, Cek8 expression is lower early in embryogenesis than at later stages. Cek8 is differentially regulated in different tissues during development and expression is highest in the nervous system but also occurs in non-neuronal tissues. In view of these results, aberrant Cek8 expression or expression of an aberrant Cek8 protein can affect development by causing defective signal transduction throughout an organism.

3. Cek8 expression and activity in tumor cells

Protein tyrosine kinase activity is tightly regulated in normal tissues and, in the tissues described above, Cek8 was phosphorylated on tyrosine at a low level. It is well known that uncontrolled tyrosine kinase activity can lead to neoplastic transformation (Bishop, J.M., Cell 64:234-248 (1991)). Therefore, the expression and activation of Cek8 in a number of tumor cell lines was examined.

Because of the predominant expression of Cek8 in the brain and retina, Cek8 expression and activity was determined in a number of cell lines, B50, B49, B35, B28 and B23, which were derived from CNS system (CNS) tumors (Schubert et al., Nature 249:224-227 (1974), which is incorporated herein by reference). B35 and B50 cells have neuronal properties and both expressed Cek8. However, Cek8 is substantially phosphorylated on tyrosine only in B50 cells (Figures 5.A. and 5.B.). B28 and B49 cells, which display glial characteristics, both expressed a moderate level of Cek8 that is phosphorylated on tyrosine. B23 cells did not have detectable levels of Cek8.

The highest level of Cek8 expression was found in undifferentiated P19 embryonal carcinoma cells (McBurney and Rogers, J. Devel. Biol. 89:503-508 (1982), which is incorporated herein by reference) and in HaCaT keratinocytes (Boukamp et al., J. Cell Biol. 106:761-770 (1988), which is incorporated herein by reference). In both of these cell lines, Cek8 was phosphorylated on tyrosine. Furthermore, comparable levels of Cek8 expression were observed in normal and Rous sarcoma virus-transformed chicken embryo fibroblasts. However, Cek8 was substantially phosphorylated on tyrosine only in the transformed cells (Figures 6.C. and 6.D.). In addition, in

LMH cells, which were derived from a hepatocellular carcinoma (Kawaguchi et al., Canc. Res. 47:4460-4464 (1987), which is incorporated herein by reference), Cek8 is highly phosphorylated on tyrosine as compared to adult or embryonic liver (Figures 6.A. and 6.B.).

For comparison, Cek5 expression and activation also was examined in the CNS tumor-derived cell lines. Cek5 was immunoprecipitated using anti-Cek5 antibodies followed by immunoblotting with anti-phosphotyrosine antibodies. Cek 5 was expressed in all of the cell lines derived from tumors of the CNS, with the highest expression in the B35 cells and the B49 cells. Tyrosine phosphorylation of Cek5 was observed in B28, B49 and B50 cells (Figures 5.C. and 5.D.). Cek5 also was highly expressed and phosphorylated in P19 cells and HaCaT cells. Thus, Cek5 expression and activation is similar, but not identical, to Cek8 expression and activation in tumor cells.

4. Effect of tyrosine phosphorylation on Cek8 kinase activity

The effect of tyrosine phosphorylation on the *in vitro* catalytic activity of Cek8 also was examined. *In vivo* substrates of Cek8 have not yet been identified. Therefore, a fusion protein consisting of the C-terminal 117 amino acids of Cek4 fused to ß-galactosidase was used as an exogenous substrate. The fusion protein was purified from bacterial extracts by SDS-PAGE and eluted from the gel.

Assays were performed by incubating 1 μg fusion protein substrate with Cek8 immunoprecipitate. Cek8 was immunoprecipitated from 10 day chick embryonic brain using 10 μg anti-Cek8 antibodies and 5 μl Staph A and was complexed to the antibodies and Staph A when the substrate was added. In some cases, Cek8 was phosphorylated for 1 hr

using the *in vitro* kinase reaction described above, in order to obtain Cek8 in a highly tyrosine-phosphorylated form. The fusion protein substrate then was added and phosphorylation of the substrate was allowed to proceed for 1 min at 0 °C or 37 °C in the phosphorylation buffer described above containing 200 μM ATP. In parallel experiments, Cek8 that was not phosphorylated *in vitro* was used in the assay.

Following incubation, the samples were centrifuged briefly in a microfuge, 100 μl 1% SDS in PBS was added to the pellets and the samples were heated at 95 °C for 5 min. The samples were centrifuged for 3 min and the supernatants were transferred to tubes containing anti-ß-galactosidase antibodies bound to Staph A beads in 900 μl RIPA buffer lacking SDS. Immunoprecipitation was performed as described above and the extent of tyrosine phosphorylation of the immunoprecipitated fusion protein substrate was analyzed by immunoblotting using anti-phosphotyrosine antibodies.

As shown in Figure 6.E., the phosphorylated form of Cek8 produced a greater amount of phosphorylation of the substrate on tyrosine at both 0 °C or 37 °C. These results indicate that activation of Cek8 by tyrosine phosphorylation increases the kinase activity of Cek8.

Although the invention has been described with reference to the disclosed embodiments, it should be understood that various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: LA JOLLA CANCER RESEARCH FOUNDATION

(ii) TITLE OF INVENTION: NOVEL EPH-RELATED TYROSINE KINASES, NUCLEOTIDE SEQUENCES, AND METHODS OF USE

(iii) NUMBER OF SEQUENCES: 26

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: CAMPBELL AND FLORES
(B) STREET: 4370 La Jolla Village Drive, Suite 700
(C) CITY: San Diego
(D) STATE: California
(E) COUNTRY: United States of America
(F) ZIP: 92122

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.25

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE: 07-Sep-1994
(C) CLASSIFICATION:

(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Imbra, Richard J.
(B) REGISTRATION NUMBER: 37,643
(C) REFERENCE/DOCKET NUMBER: FP-LJ 1114

(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: (619) 535-9001
(B) TELEFAX: (619) 535-8949

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3133 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: join(3..419, 421..2858)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

```
CA GAA ACC CTG ATG GAC ACA CGG ACA GCG ACG GCT GAG CTG GGC TGG          47
   Glu Thr Leu Met Asp Thr Arg Thr Ala Thr Ala Glu Leu Gly Trp
     1               5                  10                  15

ACT GCC AAC CCT CCG TCA GGG TGG GAA GAA GTG AGT GGC TAC GAC GAG          95
Thr Ala Asn Pro Pro Ser Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu
                 20                  25                  30
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AAC CTG AAC ACC ATC CGT ACC TAC CAG GTG TGC AAC GTC TTC GAG CCA        143
Asn Leu Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Pro
            35                  40                  45

AAC CAG AAC AAC TGG CTC CTC ACC ACC TTC ATC AAC CGG CGC GGA GCC        191
Asn Gln Asn Asn Trp Leu Leu Thr Thr Phe Ile Asn Arg Arg Gly Ala
        50                  55                  60

CAC CGC ATC TAC ACT GAG ATG CGC TTC ACT GTG CGG GAC TGC AGC AGC        239
His Arg Ile Tyr Thr Glu Met Arg Phe Thr Val Arg Asp Cys Ser Ser
    65                  70                  75

CTC CCC AAC GTC CCC GGC TCC TGC AAG GAG ACC TTC AAC CTC TAC TAC        287
Leu Pro Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr
80                  85                  90                  95

TAT GAG ACA GAC TCT GTC ATT GCC ACT AAG AAG TCG GCC TTC TGG ACG        335
Tyr Glu Thr Asp Ser Val Ile Ala Thr Lys Lys Ser Ala Phe Trp Thr
                100                 105                 110

GAG GCA CCC TAC CTC AAA GTG GAC ACC ATT GCT GCT GAC GAG AGC TTT        383
Glu Ala Pro Tyr Leu Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe
            115                 120                 125

TCC CAG GTG GAC TTT GGT GGC AGG TTG ATG AAG GGT T TTC TTC AAG          429
Ser Gln Val Asp Phe Gly Gly Arg Leu Met Lys Gly   Phe Phe Lys
        130                 135                 140

AAG TGC CCA AGC GTG GTG CAG AAC TTC GCT ATC TTC CCT GAG ACG ATG        477
Lys Cys Pro Ser Val Val Gln Asn Phe Ala Ile Phe Pro Glu Thr Met
    145                 150                 155

ACG GGG GCA GAG AGC ACC TCT CTG GTG ACA GCA CGG GGC ACC TGC ATC        525
Thr Gly Ala Glu Ser Thr Ser Leu Val Thr Ala Arg Gly Thr Cys Ile
160                 165                 170

CCC AAC GCT GAG GAG GTG GAC GTG CCC ATC AAG CTG TAC TGC AAC GGG        573
Pro Asn Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly
175                 180                 185                 190

GAT GGG GAG TGG ATG GTA CCC ATA GGT CGC TGC ACC TGC AAG GCT GGT        621
Asp Gly Glu Trp Met Val Pro Ile Gly Arg Cys Thr Cys Lys Ala Gly
                195                 200                 205

TAT GAG CCG GAA AAC AAC GTG GCT TGC AGA GCC TGC CCG GCT GGG ACA        669
Tyr Glu Pro Glu Asn Asn Val Ala Cys Arg Ala Cys Pro Ala Gly Thr
            210                 215                 220

TTC AAA GCC AGT CAG GGT GCG GGG CTG TGT GCC CGC TGT CCC CCC AAC        717
Phe Lys Ala Ser Gln Gly Ala Gly Leu Cys Ala Arg Cys Pro Pro Asn
        225                 230                 235

AGC CGC TCC AGC GCC GAG GCC TCA CCG CTC TGC GCC TGC CGC AAC GGC        765
Ser Arg Ser Ser Ala Glu Ala Ser Pro Leu Cys Ala Cys Arg Asn Gly
    240                 245                 250

TAC TTT CGG GCT GAC CTG GAC CCA CCG ACA GCT GCC TGC ACC AGC GTC        813
Tyr Phe Arg Ala Asp Leu Asp Pro Pro Thr Ala Ala Cys Thr Ser Val
255                 260                 265                 270

CCC TCT GGT CCA CGC AAC GTC ATC TCC ATT GTC AAT GAG ACC TCC ATC        861
Pro Ser Gly Pro Arg Asn Val Ile Ser Ile Val Asn Glu Thr Ser Ile
                275                 280                 285

ATC CTG GAG TGG AAC CCG CCA CGG GAG ACA GGA GGC CGG GAT GAT GTC        909
Ile Leu Glu Trp Asn Pro Pro Arg Glu Thr Gly Gly Arg Asp Asp Val
            290                 295                 300
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ACT TAC AAC ATT GTC TGC AAG AAG TGC CGG GCA GAC CGG CGT GCC TGC        957
Thr Tyr Asn Ile Val Cys Lys Lys Cys Arg Ala Asp Arg Arg Ala Cys
        305                 310                 315

TCC CGC TGC GAC GAC AAC GTG GAG TTT GTG CCC CGA CAG CTG GGG CTG       1005
Ser Arg Cys Asp Asp Asn Val Glu Phe Val Pro Arg Gln Leu Gly Leu
    320                 325                 330

ACA GAG ACC CGC GTC TTC ATC AGC AGC CTC TGG GCA CAC ACA CCC TAC       1053
Thr Glu Thr Arg Val Phe Ile Ser Ser Leu Trp Ala His Thr Pro Tyr
335                 340                 345                 350

ACC TTT GAG ATC CAG GCG GTC AAC GGG GTT TCC AAC AAG AGC CCC TTC       1101
Thr Phe Glu Ile Gln Ala Val Asn Gly Val Ser Asn Lys Ser Pro Phe
                355                 360                 365

CCA CCC CAG CAC GTC TCC GTG AAC ATC ACC ACC AAC CAA GCT GCA CCC       1149
Pro Pro Gln His Val Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro
            370                 375                 380

TCC ACT GTC CCC ATC ATG CAC CAG GTG AGT GCC ACC ATG AGG AGC ATC       1197
Ser Thr Val Pro Ile Met His Gln Val Ser Ala Thr Met Arg Ser Ile
        385                 390                 395

ACG CTA TCC TGG CCG CAG CCG GAG CAG CCC AAC GGC ATC ATC CTG GAC       1245
Thr Leu Ser Trp Pro Gln Pro Glu Gln Pro Asn Gly Ile Ile Leu Asp
    400                 405                 410

TAC GAG CTG CGC TAC TAC GAG AAG CTG AGC CGC ATC TGC ACG CCC GAT       1293
Tyr Glu Leu Arg Tyr Tyr Glu Lys Leu Ser Arg Ile Cys Thr Pro Asp
415                 420                 425                 430

GTC AGC GGC ACT GTG GGC TCG AGA CCG GCG GCG GAC CAC AAC GAG TAC       1341
Val Ser Gly Thr Val Gly Ser Arg Pro Ala Ala Asp His Asn Glu Tyr
                435                 440                 445

AAC TCC TCT GTG GCC CGC AGT CAG ACC AAC ACG GCC CGG CTG GAG GGG       1389
Asn Ser Ser Val Ala Arg Ser Gln Thr Asn Thr Ala Arg Leu Glu Gly
            450                 455                 460

CTG CGC CCT GGC ATG GTG TAC GTG GTG CAG GTG CGA GCA AGG ACG GTG       1437
Leu Arg Pro Gly Met Val Tyr Val Val Gln Val Arg Ala Arg Thr Val
        465                 470                 475

GCC GGC TAT GGG AAG TAC AGT GGG AAG ATG TGC TTC CAG ACA CTG ACC       1485
Ala Gly Tyr Gly Lys Tyr Ser Gly Lys Met Cys Phe Gln Thr Leu Thr
    480                 485                 490

GAT GAT GAC TAC AAG TCT GAG CTG AGG GAG CAG CTG CCA TTG ATT GCG       1533
Asp Asp Asp Tyr Lys Ser Glu Leu Arg Glu Gln Leu Pro Leu Ile Ala
495                 500                 505                 510

GGG TCT GCA GCG GCC GGC GTG GTC TTC ATT GTT TCG CTG GTG GCC ATT       1581
Gly Ser Ala Ala Ala Gly Val Val Phe Ile Val Ser Leu Val Ala Ile
                515                 520                 525

TCC ATA GTG TGC AGC AGG AAG CGA GCG TAC AGC AAG GAG GTC GTT TAC       1629
Ser Ile Val Cys Ser Arg Lys Arg Ala Tyr Ser Lys Glu Val Val Tyr
            530                 535                 540

AGC GAT AAG CTG CAG CAC TAC AGC ACC GGG AGA GGG TCT CCG GGA ATG       1677
Ser Asp Lys Leu Gln His Tyr Ser Thr Gly Arg Gly Ser Pro Gly Met
        545                 550                 555

AAG ATT TAC ATC GAC CCC TTC ACT TAT GAG GAC CCC AAC GAG GCA GTG       1725
Lys Ile Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val
    560                 565                 570
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CGT GAG TTC GCC AAG GAG ATT GAC GTC TCC TTT GTG AAG ATT GAA GAG      1773
Arg Glu Phe Ala Lys Glu Ile Asp Val Ser Phe Val Lys Ile Glu Glu
575                 580                 585                 590

GTC ATT GGA GCA GGG GAG TTT GGA GAG GTG TAC AAA GGC CGC CTG AAG      1821
Val Ile Gly Ala Gly Glu Phe Gly Glu Val Tyr Lys Gly Arg Leu Lys
                595                 600                 605

TTG CCT GGC AAG CGG GAG ATC TAT GTG GCC ATC AAA ACA CTG AAG GCT      1869
Leu Pro Gly Lys Arg Glu Ile Tyr Val Ala Ile Lys Thr Leu Lys Ala
            610                 615                 620

GGC TAC TCA GAG AAG CAG CGC CGG GAT TTC CTG AGC GAA GCC AGC ATC      1917
Gly Tyr Ser Glu Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile
        625                 630                 635

ATG GGG CAG TTT GAC CAC CCC AAC ATC ATC CGG CTG GAA GGG GTG GTG      1965
Met Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val
    640                 645                 650

ACC AAG AGC CGA CCA GTC ATG ATT ATC ACA GAG TTC ATG GAG AAT GGG      2013
Thr Lys Ser Arg Pro Val Met Ile Ile Thr Glu Phe Met Glu Asn Gly
655                 660                 665                 670

GCC CTG GAC TCG TTC CTG CGG CAA AAT GAT GGG CAG TTC ACA GTG ATC      2061
Ala Leu Asp Ser Phe Leu Arg Gln Asn Asp Gly Gln Phe Thr Val Ile
                675                 680                 685

CAG CTG GTG GGG ATG CTC AGA GGG ATT GCT GCT GGG ATG AAG TAC CTG      2109
Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu
            690                 695                 700

GCA GAG ATG AAC TAT GTC CAC AGG GAT CTG GCG GCC AGG AAC ATT CTG      2157
Ala Glu Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu
        705                 710                 715

GTC AAC AGC AAC CTG GTG TGC AAA GTG TCA GAC TTT GGC CTC TCG CGC      2205
Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg
    720                 725                 730

TAC CTG CAG GAC GAC ACC TCT GAT CCC ACC TAC ACC AGC TCC TTG GGT      2253
Tyr Leu Gln Asp Asp Thr Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly
735                 740                 745                 750

GGG AAG ATC CCT GTG CGA TGG ACA GCA CCA GAG GCC ATT GCG TAC CGC      2301
Gly Lys Ile Pro Val Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg
                755                 760                 765

AAG TTC ACG TCA GCC AGT GAC GTC TGG AGC TAT GGC ATC GTC ATG TGG      2349
Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp
            770                 775                 780

GAG GTG ATG TCG TTC GGA GAG AGG CCC TAC TGG GAC ATG TCC AAC CAG      2397
Glu Val Met Ser Phe Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln
        785                 790                 795

GAC GTC ATC AAT GCC ATC GAG CAG GAC TAC CGG CTC CCG CCG CCC ATG      2445
Asp Val Ile Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met
    800                 805                 810

GAC TGC CCA GCT GCC CTG CAC CAA CTG ATG CTG GAC TGC TGG CAG AAG      2493
Asp Cys Pro Ala Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys
815                 820                 825                 830

GAC CGC AAC ACC CGG CCT CGC TTG GCC GAG ATT GTC AAC ACC CTG GAC      2541
Asp Arg Asn Thr Arg Pro Arg Leu Ala Glu Ile Val Asn Thr Leu Asp
                835                 840                 845
```

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AAA ATG ATC CGC AAC CCG GCA AGC CTC AAA ACT GTG GCT ACC ATC ACC      2589
Lys Met Ile Arg Asn Pro Ala Ser Leu Lys Thr Val Ala Thr Ile Thr
            850                 855                 860

GCT GTG CCT TCT CAG CCC CTC CTC GAC CGC TCT ATC CCT GAT TTC ACT      2637
Ala Val Pro Ser Gln Pro Leu Leu Asp Arg Ser Ile Pro Asp Phe Thr
        865                 870                 875

GCC TTT ACC TCA GTA GAA GAC TGG CTG AGT GCC GTC AAG ATG AGC CAG      2685
Ala Phe Thr Ser Val Glu Asp Trp Leu Ser Ala Val Lys Met Ser Gln
    880                 885                 890

TAT AGA GAC AAC TTC CTG AGC GCT GGA TTC ACC TCC CTC CAG CTG GTC      2733
Tyr Arg Asp Asn Phe Leu Ser Ala Gly Phe Thr Ser Leu Gln Leu Val
895                 900                 905                 910

GCC CAG ATG ACA TCT GAA GAC CTC CTG AGA ATA GGA GTA ACG CTG GCT      2781
Ala Gln Met Thr Ser Glu Asp Leu Leu Arg Ile Gly Val Thr Leu Ala
                915                 920                 925

GGG CAC CAG AAG AAG ATC CTG AAC AGC ATC CAG TCC ATG CGC GTG CAG      2829
Gly His Gln Lys Lys Ile Leu Asn Ser Ile Gln Ser Met Arg Val Gln
            930                 935                 940

ATG AGT CAG TCT CCG ACC TCG ATG GCGTGACGTC CCTCGCTCGA CGAGGAGGGG     2883
Met Ser Gln Ser Pro Thr Ser Met Ala
        945                 950

GACGGGGAGG GCAGGTGGCA GAGGTGGGAG GGGAGGAACT GATCTGATGG GAGCCGTGGG    2943

GCCGCAGCTG GAGAGGGGCA GCCACGGCCG GGGCTGTGCC TGACCGCGGA GGACGTTCCT    3003

GGGACTCGCC TCGGCCTGGT GACTTCCATC CCTCACCAAC AGAAGCACAC TTACCGATGT    3063

CACGGGGGAC AGCGTATAAA TAAGTATAAA TATGTACAAA TCATATATTT AAAAAAAAAA    3123

AAAAAAAAAG                                                           3133
```

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 951 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

```
Glu Thr Leu Met Asp Thr Arg Thr Ala Thr Ala Glu Leu Gly Trp Thr
 1               5                  10                  15

Ala Asn Pro Pro Ser Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Asn
            20                  25                  30

Leu Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Pro Asn
        35                  40                  45

Gln Asn Asn Trp Leu Leu Thr Thr Phe Ile Asn Arg Arg Gly Ala His
    50                  55                  60

Arg Ile Tyr Thr Glu Met Arg Phe Thr Val Arg Asp Cys Ser Ser Leu
65                  70                  75                  80

Pro Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr
                85                  90                  95
```

```
Glu Thr Asp Ser Val Ile Ala Thr Lys Lys Ser Ala Phe Trp Thr Glu
            100                 105                 110

Ala Pro Tyr Leu Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser
        115                 120                 125

Gln Val Asp Phe Gly Gly Arg Leu Met Lys Gly Phe Phe Lys Lys Cys
    130                 135                 140

Pro Ser Val Val Gln Asn Phe Ala Ile Phe Pro Glu Thr Met Thr Gly
145                 150                 155                 160

Ala Glu Ser Thr Ser Leu Val Thr Ala Arg Gly Thr Cys Ile Pro Asn
                165                 170                 175

Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly Asp Gly
            180                 185                 190

Glu Trp Met Val Pro Ile Gly Arg Cys Thr Cys Lys Ala Gly Tyr Glu
        195                 200                 205

Pro Glu Asn Asn Val Ala Cys Arg Ala Cys Pro Ala Gly Thr Phe Lys
    210                 215                 220

Ala Ser Gln Gly Ala Gly Leu Cys Ala Arg Cys Pro Pro Asn Ser Arg
225                 230                 235                 240

Ser Ser Ala Glu Ala Ser Pro Leu Cys Ala Cys Arg Asn Gly Tyr Phe
                245                 250                 255

Arg Ala Asp Leu Asp Pro Pro Thr Ala Ala Cys Thr Ser Val Pro Ser
            260                 265                 270

Gly Pro Arg Asn Val Ile Ser Ile Val Asn Glu Thr Ser Ile Ile Leu
        275                 280                 285

Glu Trp Asn Pro Pro Arg Glu Thr Gly Gly Arg Asp Asp Val Thr Tyr
    290                 295                 300

Asn Ile Val Cys Lys Lys Cys Arg Ala Asp Arg Arg Ala Cys Ser Arg
305                 310                 315                 320

Cys Asp Asp Asn Val Glu Phe Val Pro Arg Gln Leu Gly Leu Thr Glu
                325                 330                 335

Thr Arg Val Phe Ile Ser Ser Leu Trp Ala His Thr Pro Tyr Thr Phe
            340                 345                 350

Glu Ile Gln Ala Val Asn Gly Val Ser Asn Lys Ser Pro Phe Pro Pro
        355                 360                 365

Gln His Val Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Thr
    370                 375                 380

Val Pro Ile Met His Gln Val Ser Ala Thr Met Arg Ser Ile Thr Leu
385                 390                 395                 400

Ser Trp Pro Gln Pro Glu Gln Pro Asn Gly Ile Ile Leu Asp Tyr Glu
                405                 410                 415

Leu Arg Tyr Tyr Glu Lys Leu Ser Arg Ile Cys Thr Pro Asp Val Ser
            420                 425                 430

Gly Thr Val Gly Ser Arg Pro Ala Ala Asp His Asn Glu Tyr Asn Ser
        435                 440                 445
```

```
Ser Val Ala Arg Ser Gln Thr Asn Thr Ala Arg Leu Glu Gly Leu Arg
    450                 455                 460

Pro Gly Met Val Tyr Val Val Gln Val Arg Ala Arg Thr Val Ala Gly
465                 470                 475                 480

Tyr Gly Lys Tyr Ser Gly Lys Met Cys Phe Gln Thr Leu Thr Asp Asp
                485                 490                 495

Asp Tyr Lys Ser Glu Leu Arg Glu Gln Leu Pro Leu Ile Ala Gly Ser
            500                 505                 510

Ala Ala Ala Gly Val Val Phe Ile Val Ser Leu Val Ala Ile Ser Ile
        515                 520                 525

Val Cys Ser Arg Lys Arg Ala Tyr Ser Lys Glu Val Val Tyr Ser Asp
    530                 535                 540

Lys Leu Gln His Tyr Ser Thr Gly Arg Gly Ser Pro Gly Met Lys Ile
545                 550                 555                 560

Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu
                565                 570                 575

Phe Ala Lys Glu Ile Asp Val Ser Phe Val Lys Ile Glu Glu Val Ile
            580                 585                 590

Gly Ala Gly Glu Phe Gly Glu Val Tyr Lys Gly Arg Leu Lys Leu Pro
        595                 600                 605

Gly Lys Arg Glu Ile Tyr Val Ala Ile Lys Thr Leu Lys Ala Gly Tyr
    610                 615                 620

Ser Glu Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly
625                 630                 635                 640

Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr Lys
                645                 650                 655

Ser Arg Pro Val Met Ile Ile Thr Glu Phe Met Glu Asn Gly Ala Leu
            660                 665                 670

Asp Ser Phe Leu Arg Gln Asn Asp Gly Gln Phe Thr Val Ile Gln Leu
        675                 680                 685

Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala Glu
    690                 695                 700

Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn
705                 710                 715                 720

Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Tyr Leu
                725                 730                 735

Gln Asp Asp Thr Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly Gly Lys
            740                 745                 750

Ile Pro Val Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg Lys Phe
        755                 760                 765

Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val
    770                 775                 780

Met Ser Phe Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val
785                 790                 795                 800
```

```
Ile Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys
                805                 810                 815

Pro Ala Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg
            820                 825                 830

Asn Thr Arg Pro Arg Leu Ala Glu Ile Val Asn Thr Leu Asp Lys Met
        835                 840                 845

Ile Arg Asn Pro Ala Ser Leu Lys Thr Val Ala Thr Ile Thr Ala Val
    850                 855                 860

Pro Ser Gln Pro Leu Leu Asp Arg Ser Ile Pro Asp Phe Thr Ala Phe
865                 870                 875                 880

Thr Ser Val Glu Asp Trp Leu Ser Ala Val Lys Met Ser Gln Tyr Arg
                885                 890                 895

Asp Asn Phe Leu Ser Ala Gly Phe Thr Ser Leu Gln Leu Val Ala Gln
            900                 905                 910

Met Thr Ser Glu Asp Leu Leu Arg Ile Gly Val Thr Leu Ala Gly His
        915                 920                 925

Gln Lys Lys Ile Leu Asn Ser Ile Gln Ser Met Arg Val Gln Met Ser
    930                 935                 940

Gln Ser Pro Thr Ser Met Ala
945                 950
```

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3059 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..2167

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

```
C CTC AAA TTC ACC CTG AGG GAC TGT AAC AGC CTT CCA GGA GGA CTT          46
  Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu
    1               5                  10                  15

GGG ACT TGC AAG GAG ACT TTT AAC ATG TAC TAC TTT GAG TCA GAT GAT          94
Gly Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp
                20                  25                  30

GAA GAT GGG AGG AAC ATC AGA GAG AAT CAG TAC ATC AAG ATA GAT ACC         142
Glu Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr
            35                  40                  45

ATT GCT GCT GAT GAG AGC TTC ACG GAG TTG GAC CTC GGC GAC AGA GTT         190
Ile Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val
        50                  55                  60

ATG AAG TTA AAC ACA GAA GTG AGA GAT GTT GGG CCT CTA ACA AAA AAA         238
Met Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys
    65                  70                  75
```

```
GGA TTT TAC CTT GCT TTC CAG GAT GTG GGC GCC TGC ATT GCC CTG GTC        286
Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val
 80                  85                  90                  95

TCT GTG CGT GTG TAC TAC AAG AAA TGC CCA TCA GTG ATC CGC AAC CTG        334
Ser Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu
                100                 105                 110

GCA CGC TTT CCA GAT ACC ATC ACA GGA GCA GAT TCC TCG CAG CTG CTA        382
Ala Arg Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu
            115                 120                 125

GAA GTG TCA GGC GTC TGT GTC AAC CAC TCA GTG ACT GAT GAG GCA CCA        430
Glu Val Ser Gly Val Cys Val Asn His Ser Val Thr Asp Glu Ala Pro
        130                 135                 140

AAG ATG CAC TGC AGT TCA GAG GGA GAA TGG CTG GTG CCC ATT GGG AAG        478
Lys Met His Cys Ser Ser Glu Gly Glu Trp Leu Val Pro Ile Gly Lys
    145                 150                 155

TGT TTG TGC AAG GCA GGG TAC GAG GAG AAG AAC AAC ACC TGC CAA GCA        526
Cys Leu Cys Lys Ala Gly Tyr Glu Glu Lys Asn Asn Thr Cys Gln Ala
160                 165                 170                 175

CCT TCT CCA GTC AGT AGT GTG AAA AAA GGG AAG ATA ACT AAA AAT AGC        574
Pro Ser Pro Val Ser Ser Val Lys Lys Gly Lys Ile Thr Lys Asn Ser
                180                 185                 190

ATC TCC CTT TCC TGG CAG GAG CCA GAT CGA CCC AAC GGC ATC ATC CTG        622
Ile Ser Leu Ser Trp Gln Glu Pro Asp Arg Pro Asn Gly Ile Ile Leu
            195                 200                 205

GAA TAC GAA ATC AAA TAT TTT GAA AAG GAC CAG GAG ACA AGC TAC ACC        670
Glu Tyr Glu Ile Lys Tyr Phe Glu Lys Asp Gln Glu Thr Ser Tyr Thr
        210                 215                 220

ATC ATC AAA TCC AAA GAG ACC GCA ATT ACG GCA GAT GGC TTG AAA CCA        718
Ile Ile Lys Ser Lys Glu Thr Ala Ile Thr Ala Asp Gly Leu Lys Pro
    225                 230                 235

GGC TCA GCG TAC GTC TTC CAG ATC CGA GCC CGG ACA GCT GCT GGC TAC        766
Gly Ser Ala Tyr Val Phe Gln Ile Arg Ala Arg Thr Ala Ala Gly Tyr
240                 245                 250                 255

GGT GGC TTC AGT CGA AGA TTT GAG TTT GAA ACC AGC CCA GTG TTA GCT        814
Gly Gly Phe Ser Arg Arg Phe Glu Phe Glu Thr Ser Pro Val Leu Ala
                260                 265                 270

GCA TCC AGT GAC CAG AGC CAG ATT CCT ATA ATT GTT GTG TCT GTA ACA        862
Ala Ser Ser Asp Gln Ser Gln Ile Pro Ile Ile Val Val Ser Val Thr
            275                 280                 285

GTG GGA GTT ATT CTG CTG GCT GTT GTT ATC GGT TTC CTT CTC AGT GGA        910
Val Gly Val Ile Leu Leu Ala Val Val Ile Gly Phe Leu Leu Ser Gly
        290                 295                 300

AGG CGC TGT GGC TAC AGC AAG GCT AAA CAA GAC CCA GAA GAA GAA AAG        958
Arg Arg Cys Gly Tyr Ser Lys Ala Lys Gln Asp Pro Glu Glu Glu Lys
    305                 310                 315

ATG CAT TTT CAT AAT GGC CAC ATT AAA CTG CCT GGT GTA AGA ACC TAC       1006
Met His Phe His Asn Gly His Ile Lys Leu Pro Gly Val Arg Thr Tyr
320                 325                 330                 335

ATT GAT CCC CAC ACC TAT GAG GAC CCT AAT CAA GCT GTC CAC GAG TTT       1054
Ile Asp Pro His Thr Tyr Glu Asp Pro Asn Gln Ala Val His Glu Phe
                340                 345                 350
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GCC AAG GAA ATA GAA GCT TCG TGC ATA ACC ATC GAG AGA GTT ATC GGA      1102
Ala Lys Glu Ile Glu Ala Ser Cys Ile Thr Ile Glu Arg Val Ile Gly
            355                 360                 365

GCT GGT GAA TTT GGA GAA GTC TGC AGT GGA CGG CTG AAA CTG CAG GGA      1150
Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Gln Gly
        370                 375                 380

AAA CGC GAG TTT CCA GTG GCT ATC AAA ACC CTG AAG GTG GGC TAC ACA      1198
Lys Arg Glu Phe Pro Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr
    385                 390                 395

GAG AAG CAA AGG CGA GAT TTC CTG GGA GAA GCG AGC ATC ATG GGG CAG      1246
Glu Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser Ile Met Gly Gln
400                 405                 410                 415

TTC GAC CAC CCC AAC ATC ATC CAC CTG GAA GGT GTC GTC ACA AAA AGC      1294
Phe Asp His Pro Asn Ile Ile His Leu Glu Gly Val Val Thr Lys Ser
                420                 425                 430

AAA CCT GTA ATG ATA GTA ACG GAA TAC ATG GAA AAT GGT TCT CTG GAT      1342
Lys Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp
            435                 440                 445

ACA TTT TTA AAG AAG AAC GAT GGG CAG TTC ACG GTC ATT CAG CTG GTC      1390
Thr Phe Leu Lys Lys Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val
        450                 455                 460

GGG ATG CTG CGA GGC ATC GCA TCA GGG ATG AAG TAC CTG TCT GAC ATG      1438
Gly Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr Leu Ser Asp Met
    465                 470                 475

GGT TAC GTA CAC AGA GAC CTC GCT GCC AGG AAT ATC CTC ATC AAC AGC      1486
Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Ile Asn Ser
480                 485                 490                 495

AAC TTA GTC TGC AAG GTG TCT GAC TTT GGC CTC TCC AGA GTC CTA GAA      1534
Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu
                500                 505                 510

GAT GAT CCT GAA GCA GCG TAC ACA ACC AGG GGA GGG AAG ATC CCC ATC      1582
Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile
            515                 520                 525

CGA TGG ACG GCA CCT GAA GCA ATC GCC TTC CGC AAA TTC ACG TCG GCC      1630
Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala
        530                 535                 540

AGC GAT GTG TGG AGC TAC GGC ATT GTG ATG TGG GAA GTG ATG TCC TAT      1678
Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr
    545                 550                 555

GGC GAG AGA CCT TAC TGG GAA ATG ACA AAC CAA GAT GTG ATT AAA GCC      1726
Gly Glu Arg Pro Tyr Trp Glu Met Thr Asn Gln Asp Val Ile Lys Ala
560                 565                 570                 575

GTG GAG GAA GGC TAT CGC CTG CCA AGT CCC ATG GAC TGC CCT GCT GCT      1774
Val Glu Glu Gly Tyr Arg Leu Pro Ser Pro Met Asp Cys Pro Ala Ala
                580                 585                 590

CTC TAC CAG TTG ATG CTT GAC TGC TGG CAG AAA GAC CGC AAC AGC AGG      1822
Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Ser Arg
            595                 600                 605

CCC AAG TTT GAT GAA ATT GTC AGC ATG TTG GAC AAG CTC ATC CGT AAC      1870
Pro Lys Phe Asp Glu Ile Val Ser Met Leu Asp Lys Leu Ile Arg Asn
        610                 615                 620
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CCA AGC AGC TTG AAG ACG TTG GTT AAT GCA TCG AGC AGA GTA TCA AAT      1918
Pro Ser Ser Leu Lys Thr Leu Val Asn Ala Ser Ser Arg Val Ser Asn
    625                 630                 635

TTG TTG GTA GAA CAC AGT CCA GTG GGG AGC GGT GCC TAC AGG TCA GTG      1966
Leu Leu Val Glu His Ser Pro Val Gly Ser Gly Ala Tyr Arg Ser Val
640                 645                 650                 655

GGT GAG TGG CTG GAA GCC ATC AAA ATG GGT CGA TAC ACC GAG ATT TTC      2014
Gly Glu Trp Leu Glu Ala Ile Lys Met Gly Arg Tyr Thr Glu Ile Phe
                660                 665                 670

ATG GAG AAT GGA TAC AGT TCG ATG GAT TCT GTG GCT CAG GTG ACC CTA      2062
Met Glu Asn Gly Tyr Ser Ser Met Asp Ser Val Ala Gln Val Thr Leu
            675                 680                 685

GAG GAT TTG AGG CGG CTG GGA GTG ACA CTT GTT GGT CAC CAG AAG AAG      2110
Glu Asp Leu Arg Arg Leu Gly Val Thr Leu Val Gly His Gln Lys Lys
        690                 695                 700

ATA ATG AAC AGC CTT CAA GAG ATG AAG GTC CAG TTG GTG AAT GGG ATG      2158
Ile Met Asn Ser Leu Gln Glu Met Lys Val Gln Leu Val Asn Gly Met
    705                 710                 715

GTG CCA TTG TAACTCGGTT TTTAAGTCAC TTCCTCGAGT GGTCGGTCCT              2207
Val Pro Leu
720

GCACTTTGTA TACTAGCTCT GAGATTTATT TTGACTAAAG AAGAAAAAAG GGAAATTCAG    2267

TGGTTTCTGT AACTGAAGGA CGCTGGCTTC TGCCACAGCA TTTATAAAGC AGTGTTTGAC    2327

TGAAGTTTTC ATTTTCTTCC TATTTGTGTC CTCATTCTCA TGAAGTAAAT GTAACATGCA    2387

TGGAACATGG AAATGGATCT ACTGTACATG AGGTTACCCA ATTTCTTGCG CTTCAGCATG    2447

ACAACAGCAA GCCTTCCCAC CACATGTTGT CTATACATGG GAGATATATA TATATGCATA    2507

TATATATATA GCACCTTTAT ATACTGAATT ACAGCAGCAG CACATGTTAA TACTTCCAAG    2567

GACTTACTTG ACTAGAGAAG TTTTGCAGCC ATTGTGGGCT CACACAAGCT GCGGTTTACT    2627

GAAGTTTACT TCAAGTCTTA CTTGTCTACA GAAGTGTATT GAAGAGCAAT ATGATTAGAT    2687

TATTTCTGGA TAGATATTTT GTTTTGTAAA TTTAAAAAAT CGTGTTACAC AGCGTTAAGT    2747

TATAGAGACT AGTGTATAAA CATGTTGCTT GCTCAATGGC AAATACAATA CAGGGTGTAT    2807

ATTTTTTTCT CTCTGTGTTG CAAAGTTCTT TTAGTTTGCT CTTCTGTGAG GATAATACGT    2867

TATGATGTAT ATACTGTACA GTTTGCTACA CATCAGGTAC AAGATTGGGG CTTTCTCAAT    2927

GTTTTGTTCT TTTTCCCTCT TTTGTTTCAT TTTGTCTTCC TTTTGTGTTA ACCACTATGC    2987

TTTGTATTTT TGCTGCTGTT TGGTTTGAGG CAACATATAA AGCTTTCAGG TGTTTTGATT    3047

ATAAAAAAAA AG                                                        3059
```

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 722 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```
Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu Gly
 1               5                  10                  15

Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp Glu
            20                  25                  30

Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr Ile
        35                  40                  45

Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val Met
    50                  55                  60

Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys Gly
65                  70                  75                  80

Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val Ser
                85                  90                  95

Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu Ala
            100                 105                 110

Arg Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu Glu
        115                 120                 125

Val Ser Gly Val Cys Val Asn His Ser Val Thr Asp Glu Ala Pro Lys
    130                 135                 140

Met His Cys Ser Ser Glu Gly Glu Trp Leu Val Pro Ile Gly Lys Cys
145                 150                 155                 160

Leu Cys Lys Ala Gly Tyr Glu Glu Lys Asn Asn Thr Cys Gln Ala Pro
                165                 170                 175

Ser Pro Val Ser Ser Val Lys Lys Gly Lys Ile Thr Lys Asn Ser Ile
            180                 185                 190

Ser Leu Ser Trp Gln Glu Pro Asp Arg Pro Asn Gly Ile Ile Leu Glu
        195                 200                 205

Tyr Glu Ile Lys Tyr Phe Glu Lys Asp Gln Glu Thr Ser Tyr Thr Ile
    210                 215                 220

Ile Lys Ser Lys Glu Thr Ala Ile Thr Ala Asp Gly Leu Lys Pro Gly
225                 230                 235                 240

Ser Ala Tyr Val Phe Gln Ile Arg Ala Arg Thr Ala Ala Gly Tyr Gly
                245                 250                 255

Gly Phe Ser Arg Arg Phe Glu Phe Glu Thr Ser Pro Val Leu Ala Ala
            260                 265                 270

Ser Ser Asp Gln Ser Gln Ile Pro Ile Ile Val Val Ser Val Thr Val
        275                 280                 285

Gly Val Ile Leu Leu Ala Val Val Ile Gly Phe Leu Leu Ser Gly Arg
    290                 295                 300
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Arg Cys Gly Tyr Ser Lys Ala Lys Gln Asp Pro Glu Glu Glu Lys Met
305                 310                 315                 320

His Phe His Asn Gly His Ile Lys Leu Pro Gly Val Arg Thr Tyr Ile
                325                 330                 335

Asp Pro His Thr Tyr Glu Asp Pro Asn Gln Ala Val His Glu Phe Ala
            340                 345                 350

Lys Glu Ile Glu Ala Ser Cys Ile Thr Ile Glu Arg Val Ile Gly Ala
        355                 360                 365

Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Gln Gly Lys
    370                 375                 380

Arg Glu Phe Pro Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr Glu
385                 390                 395                 400

Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser Ile Met Gly Gln Phe
                405                 410                 415

Asp His Pro Asn Ile Ile His Leu Glu Gly Val Val Thr Lys Ser Lys
            420                 425                 430

Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Thr
        435                 440                 445

Phe Leu Lys Lys Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly
    450                 455                 460

Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr Leu Ser Asp Met Gly
465                 470                 475                 480

Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Ile Asn Ser Asn
                485                 490                 495

Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu Asp
            500                 505                 510

Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg
        515                 520                 525

Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala Ser
    530                 535                 540

Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly
545                 550                 555                 560

Glu Arg Pro Tyr Trp Glu Met Thr Asn Gln Asp Val Ile Lys Ala Val
                565                 570                 575

Glu Glu Gly Tyr Arg Leu Pro Ser Pro Met Asp Cys Pro Ala Ala Leu
            580                 585                 590

Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Ser Arg Pro
        595                 600                 605

Lys Phe Asp Glu Ile Val Ser Met Leu Asp Lys Leu Ile Arg Asn Pro
    610                 615                 620

Ser Ser Leu Lys Thr Leu Val Asn Ala Ser Ser Arg Val Ser Asn Leu
625                 630                 635                 640

Leu Val Glu His Ser Pro Val Gly Ser Gly Ala Tyr Arg Ser Val Gly
                645                 650                 655
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Glu Trp Leu Glu Ala Ile Lys Met Gly Arg Tyr Thr Glu Ile Phe Met
           660                 665                 670

Glu Asn Gly Tyr Ser Ser Met Asp Ser Val Ala Gln Val Thr Leu Glu
       675                 680                 685

Asp Leu Arg Arg Leu Gly Val Thr Leu Val Gly His Gln Lys Lys Ile
   690                 695                 700

Met Asn Ser Leu Gln Glu Met Lys Val Gln Leu Val Asn Gly Met Val
705                 710                 715                 720

Pro Leu
```

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2820 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..2548

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

```
C GGA GAG AGC CAG TTT GCC AAG ATT GAC ACC ATT GCT GCT GAT GAG          46
  Gly Glu Ser Gln Phe Ala Lys Ile Asp Thr Ile Ala Ala Asp Glu
   1               5                  10                  15

AGC TTC ACC CAG GTG GAC ATT GGT GAC AGG ATC ATG AAG CTG AAT ACA        94
Ser Phe Thr Gln Val Asp Ile Gly Asp Arg Ile Met Lys Leu Asn Thr
               20                  25                  30

GAG GTG CGG GAC GTG GGG CCT CTC AGC AAG AAA GGG TTT TAC TTG GCT       142
Glu Val Arg Asp Val Gly Pro Leu Ser Lys Lys Gly Phe Tyr Leu Ala
           35                  40                  45

TTC CAG GAC GTC GGT GCC TGC ATT GCT TTG GTG TCT GTT CGT GTC TTC       190
Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val Ser Val Arg Val Phe
       50                  55                  60

TAT AAG AAG TGC CCA CTG ACA GTT CGA AAC CTG GCA CAG TTT CCA GAC       238
Tyr Lys Lys Cys Pro Leu Thr Val Arg Asn Leu Ala Gln Phe Pro Asp
   65                  70                  75

ACC ATT ACT GGG GCT GAT ACA TCC TCT CTG GTG GAG GTT CGT GGC TCC       286
Thr Ile Thr Gly Ala Asp Thr Ser Ser Leu Val Glu Val Arg Gly Ser
80                  85                  90                  95

TGT GTC AAC AAC TCG GAA GAG AAG GAC GTG CCA AAA ATG TAC TGC GGG       334
Cys Val Asn Asn Ser Glu Glu Lys Asp Val Pro Lys Met Tyr Cys Gly
               100                 105                 110

GCA GAT GGT GAA TGG CTG GTA CCC ATT GGC AAC TGT CTG TGC AAT GCT       382
Ala Asp Gly Glu Trp Leu Val Pro Ile Gly Asn Cys Leu Cys Asn Ala
           115                 120                 125

GGC TAT GAA GAA CGC AAT GGT GAA TGC CAA GCT TGC AAA ATC GGA TAC       430
Gly Tyr Glu Glu Arg Asn Gly Glu Cys Gln Ala Cys Lys Ile Gly Tyr
       130                 135                 140
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TAC AAG GCG CTC TCA ACA GAT GTT GCA TGT GCC AAA TGC CCG CCT CAC        478
Tyr Lys Ala Leu Ser Thr Asp Val Ala Cys Ala Lys Cys Pro Pro His
    145                 150                 155

AGC TAC TCC ATC TGG GAA GGC TCT ACC TCC TGC ACC TGT GAT CGG GGC        526
Ser Tyr Ser Ile Trp Glu Gly Ser Thr Ser Cys Thr Cys Asp Arg Gly
160                 165                 170                 175

TTC TTC CGA GCA GAA AAT GAT GCT GCA TCC ATG CCC TGC ACT CGC CCT        574
Phe Phe Arg Ala Glu Asn Asp Ala Ala Ser Met Pro Cys Thr Arg Pro
                180                 185                 190

CCA TCC GCA CCC CAG AAC CTG ATT TCC AAC GTC AAC GAG ACG TCA GTG        622
Pro Ser Ala Pro Gln Asn Leu Ile Ser Asn Val Asn Glu Thr Ser Val
            195                 200                 205

AAC TTG GAG TGG AGC GCC CCA CAG AAC AAG GGA GGA CGG GAC GAC ATC        670
Asn Leu Glu Trp Ser Ala Pro Gln Asn Lys Gly Gly Arg Asp Asp Ile
        210                 215                 220

TCC TAC AAC GTG GTG TGC AAG CGC TGC GGG GCA GGG GAG CCC AGC CAC        718
Ser Tyr Asn Val Val Cys Lys Arg Cys Gly Ala Gly Glu Pro Ser His
    225                 230                 235

TGC CGG TCC TGT GGC AGT GGT GTA CAT TTC AGC CCC CAG CAG AAC GGG        766
Cys Arg Ser Cys Gly Ser Gly Val His Phe Ser Pro Gln Gln Asn Gly
240                 245                 250                 255

CTG AAA ACC ACG AAG GTT TCC ATC ACT GAC CTC CTG GCA CAC ACC AAC        814
Leu Lys Thr Thr Lys Val Ser Ile Thr Asp Leu Leu Ala His Thr Asn
                260                 265                 270

TAC ACC TTT GAG GTC TGG GCA GTG AAT GGA GTG TCC AAG CAC AAC CCC        862
Tyr Thr Phe Glu Val Trp Ala Val Asn Gly Val Ser Lys His Asn Pro
            275                 280                 285

AGC CAG GAC CAA GCT GTG TCG GTC ACT GTG ACA ACT AAC CAA GCA GCT        910
Ser Gln Asp Gln Ala Val Ser Val Thr Val Thr Thr Asn Gln Ala Ala
        290                 295                 300

CCA TCC CCA ATT GCA TTG ATC CAG GCT AAA GAG ATA ACG AGG CAC AGC        958
Pro Ser Pro Ile Ala Leu Ile Gln Ala Lys Glu Ile Thr Arg His Ser
    305                 310                 315

GTT GCC TTG GCC TGG CTG GAA CCT GAC AGG CCC AAT GGA GTC ATC CTG       1006
Val Ala Leu Ala Trp Leu Glu Pro Asp Arg Pro Asn Gly Val Ile Leu
320                 325                 330                 335

GAG TAC GAA GTC AAG TAC TAC GAA AAG GAC CAA AAC GAG CGC ACG TAT       1054
Glu Tyr Glu Val Lys Tyr Tyr Glu Lys Asp Gln Asn Glu Arg Thr Tyr
                340                 345                 350

CGC ATT GTG AAG ACA GCC TCC AGG AAT ACT GAC ATC AAA GGT TTG AAC       1102
Arg Ile Val Lys Thr Ala Ser Arg Asn Thr Asp Ile Lys Gly Leu Asn
            355                 360                 365

CCC CTG ACT TCA TAT GTA TTT CAT GTG CGG GCC AGG ACA GCA GCA GGA       1150
Pro Leu Thr Ser Tyr Val Phe His Val Arg Ala Arg Thr Ala Ala Gly
        370                 375                 380

TAC GGA GAC TTC AGT GGG CCG TTT GAG TTC ACA ACT AAC ACA GTT CCT       1198
Tyr Gly Asp Phe Ser Gly Pro Phe Glu Phe Thr Thr Asn Thr Val Pro
    385                 390                 395

TCC CCC ATC ATT GGC GAT GGT ACC AAT CCC ACA GTG CTG CTT GTT TCA       1246
Ser Pro Ile Ile Gly Asp Gly Thr Asn Pro Thr Val Leu Leu Val Ser
400                 405                 410                 415
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GTG GCT GGC AGT GTT GTT CTT GTG GTC ATT CTC ATT GCA GCC TTT GTC      1294
Val Ala Gly Ser Val Val Leu Val Val Ile Leu Ile Ala Ala Phe Val
                420                 425                 430

ATC AGC AGG AGG CGC AGC AAA TAC AGT AAA GCT AAG CAA GAG GCA GAT      1342
Ile Ser Arg Arg Arg Ser Lys Tyr Ser Lys Ala Lys Gln Glu Ala Asp
            435                 440                 445

GAG GAG AAA CAT TTG AAC CAA GGT GTC AGA ACA TAT GTG GAT CCT TTT      1390
Glu Glu Lys His Leu Asn Gln Gly Val Arg Thr Tyr Val Asp Pro Phe
        450                 455                 460

ACA TAT GAG GAT CCA AAT CAA GCT GTG AGG GAA TTT GCC AAA GAA ATT      1438
Thr Tyr Glu Asp Pro Asn Gln Ala Val Arg Glu Phe Ala Lys Glu Ile
    465                 470                 475

GAT GCC TCC TGC ATA AAG ATT GAG AAA GTT ATT GGT GTG GGG GAA TTT      1486
Asp Ala Ser Cys Ile Lys Ile Glu Lys Val Ile Gly Val Gly Glu Phe
480                 485                 490                 495

GGT GAA GTA TGC AGT GGA CGT CTC AAA GTT CCA GGA AAA AGA GAA ATC      1534
Gly Glu Val Cys Ser Gly Arg Leu Lys Val Pro Gly Lys Arg Glu Ile
                500                 505                 510

TGT GTG GCT ATC AAG ACT CTG AAA GCT GGT TAC ACT GAC AAA CAA CGG      1582
Cys Val Ala Ile Lys Thr Leu Lys Ala Gly Tyr Thr Asp Lys Gln Arg
            515                 520                 525

AGA GAC TTC CTG AGT GAG GCC AGC ATC ATG GGA CAA TTT GAC CAC CCC      1630
Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro
        530                 535                 540

AAT ATC ATC CAC TTG GAA GGC GTT GTT ACT AAA TGT AAA CCA GTA ATG      1678
Asn Ile Ile His Leu Glu Gly Val Val Thr Lys Cys Lys Pro Val Met
    545                 550                 555

ATC ATA ACT GAG TAC ATG GAG AAT GGC TCC TTG GAT GCC TTC CTC CGG      1726
Ile Ile Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Ala Phe Leu Arg
560                 565                 570                 575

AAG AAT GAT GGC AGA TTT ACA GTA ATC CAG TTG GTG GGG ATG CTT CGT      1774
Lys Asn Asp Gly Arg Phe Thr Val Ile Gln Leu Val Gly Met Leu Arg
                580                 585                 590

GGC ATC GGC TCA GGA ATG AAG TAT CTG TCT GAC ATG AGC TAT GTG CAT      1822
Gly Ile Gly Ser Gly Met Lys Tyr Leu Ser Asp Met Ser Tyr Val His
            595                 600                 605

CGG GAT CTA GCT GCT CGA AAC ATA CTG GTC AAC AGC AAC TTG GTC TGC      1870
Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val Cys
        610                 615                 620

AAA GTG TCT GAC TTT GGC ATG TCC CGT GTC CTG GAA GAT GAC CCT GAG      1918
Lys Val Ser Asp Phe Gly Met Ser Arg Val Leu Glu Asp Asp Pro Glu
    625                 630                 635

GCA GCT TAT ACC ACA CGG GGT GGC AAG ATC CCT ATC CGA TGG ACT GCA      1966
Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala
640                 645                 650                 655

CCA GAG GCA ATT GCC TAC CGT AAA TTT ACA TCG GCT AGT GAC GTG TGG      2014
Pro Glu Ala Ile Ala Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val Trp
                660                 665                 670

AGC TAT GGC ATC GTC ATG TGG GAA GTG ATG TCC TAT GGA GAG AGA CCT      2062
Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro
            675                 680                 685
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TAC TGG GAT ATG TCC AAT CAA GAC GTT ATT AAA GCC ATT GAG GAA GGG      2110
Tyr Trp Asp Met Ser Asn Gln Asp Val Ile Lys Ala Ile Glu Glu Gly
        690                 695                 700

TAT CGG TTG CCA CCC CCA ATG GAC TGC CCC ATT GCT CTC CAT CAG CTG      2158
Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro Ile Ala Leu His Gln Leu
    705                 710                 715

ATG TTA GAC TGC TGG CAG AAG GAA CGC AGC GAC AGA CCT AAA TTT GGA      2206
Met Leu Asp Cys Trp Gln Lys Glu Arg Ser Asp Arg Pro Lys Phe Gly
720                 725                 730                 735

CAG ATT GTC AAC ATG CTG GAC AAA CTC ATC CGC AAC CCT AAC AGC CTG      2254
Gln Ile Val Asn Met Leu Asp Lys Leu Ile Arg Asn Pro Asn Ser Leu
                740                 745                 750

AAG AGG ACA GGC AGC GAG AGC TCC AGA CCC AGC ACA GCC CTG CTG GAT      2302
Lys Arg Thr Gly Ser Glu Ser Ser Arg Pro Ser Thr Ala Leu Leu Asp
            755                 760                 765

CCC AGC TCC CCG GAG TTC TCG GCG GTT GTT TCT GTC AGT GAC TGG CTC      2350
Pro Ser Ser Pro Glu Phe Ser Ala Val Val Ser Val Ser Asp Trp Leu
        770                 775                 780

CAA GCC ATT AAA ATG GAG CGA TAC AAG GAT AAC TTC ACA GCT GCT GGC      2398
Gln Ala Ile Lys Met Glu Arg Tyr Lys Asp Asn Phe Thr Ala Ala Gly
    785                 790                 795

TAT ACC ACC CTA GAG GCT GTG GTG CAT ATG AAC CAG GAC GAC CTG GCC      2446
Tyr Thr Thr Leu Glu Ala Val Val His Met Asn Gln Asp Asp Leu Ala
800                 805                 810                 815

AGG ATC GGG ATC ACT GCC ATC ACA CAC CAG AAC AAG ATC TTG AGC AGC      2494
Arg Ile Gly Ile Thr Ala Ile Thr His Gln Asn Lys Ile Leu Ser Ser
                820                 825                 830

GTT CAA GCC ATG CGC AGC CAA ATG CAA CAG ATG CAC GGC AGG ATG GTG      2542
Val Gln Ala Met Arg Ser Gln Met Gln Gln Met His Gly Arg Met Val
            835                 840                 845

CCC GTC TGAGCCAGTA CTGAATAAAC TCAAAACTCT TGAAATTAGT TTACCTCATC      2598
Pro Val

CATGCACTTT AATTGAAGAA CTGCACTTTT TTTACTTCGT CTCCTCGCCC GTTGAAATAA   2658

AGATCTGCAG CATTGCTTGA TGTACAGATT GTGGAAACCG AGCGTGTGTT GGGAGGGGGG   2718

CCTCCAGAAA TGACAAGCCG TCATTTTAAA CCAGACCTGG AACAAATTGT TTCTTGGAAC   2778

ATACTTCTCT GTTGATCAAC GATATGTAAA ATACATGTAT CC                      2820
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(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 849 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

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Gly Glu Ser Gln Phe Ala Lys Ile Asp Thr Ile Ala Ala Asp Glu Ser
  1               5                  10                  15
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Phe Thr Gln Val Asp Ile Gly Asp Arg Ile Met Lys Leu Asn Thr Glu
            20                  25                  30

Val Arg Asp Val Gly Pro Leu Ser Lys Lys Gly Phe Tyr Leu Ala Phe
        35                  40                  45

Gln Asp Val Gly Ala Cys Ile Ala Leu Val Ser Val Arg Val Phe Tyr
    50                  55                  60

Lys Lys Cys Pro Leu Thr Val Arg Asn Leu Ala Gln Phe Pro Asp Thr
65                  70                  75                  80

Ile Thr Gly Ala Asp Thr Ser Ser Leu Val Glu Val Arg Gly Ser Cys
                85                  90                  95

Val Asn Asn Ser Glu Glu Lys Asp Val Pro Lys Met Tyr Cys Gly Ala
            100                 105                 110

Asp Gly Glu Trp Leu Val Pro Ile Gly Asn Cys Leu Cys Asn Ala Gly
        115                 120                 125

Tyr Glu Glu Arg Asn Gly Glu Cys Gln Ala Cys Lys Ile Gly Tyr Tyr
    130                 135                 140

Lys Ala Leu Ser Thr Asp Val Ala Cys Ala Lys Cys Pro Pro His Ser
145                 150                 155                 160

Tyr Ser Ile Trp Glu Gly Ser Thr Ser Cys Thr Cys Asp Arg Gly Phe
                165                 170                 175

Phe Arg Ala Glu Asn Asp Ala Ala Ser Met Pro Cys Thr Arg Pro Pro
            180                 185                 190

Ser Ala Pro Gln Asn Leu Ile Ser Asn Val Asn Glu Thr Ser Val Asn
        195                 200                 205

Leu Glu Trp Ser Ala Pro Gln Asn Lys Gly Gly Arg Asp Asp Ile Ser
    210                 215                 220

Tyr Asn Val Val Cys Lys Arg Cys Gly Ala Gly Glu Pro Ser His Cys
225                 230                 235                 240

Arg Ser Cys Gly Ser Gly Val His Phe Ser Pro Gln Gln Asn Gly Leu
                245                 250                 255

Lys Thr Thr Lys Val Ser Ile Thr Asp Leu Leu Ala His Thr Asn Tyr
            260                 265                 270

Thr Phe Glu Val Trp Ala Val Asn Gly Val Ser Lys His Asn Pro Ser
        275                 280                 285

Gln Asp Gln Ala Val Ser Val Thr Val Thr Thr Asn Gln Ala Ala Pro
    290                 295                 300

Ser Pro Ile Ala Leu Ile Gln Ala Lys Glu Ile Thr Arg His Ser Val
305                 310                 315                 320

Ala Leu Ala Trp Leu Glu Pro Asp Arg Pro Asn Gly Val Ile Leu Glu
                325                 330                 335

Tyr Glu Val Lys Tyr Tyr Glu Lys Asp Gln Asn Glu Arg Thr Tyr Arg
            340                 345                 350

Ile Val Lys Thr Ala Ser Arg Asn Thr Asp Ile Lys Gly Leu Asn Pro
        355                 360                 365
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Leu Thr Ser Tyr Val Phe His Val Arg Ala Arg Thr Ala Ala Gly Tyr
    370                 375                 380

Gly Asp Phe Ser Gly Pro Phe Glu Phe Thr Thr Asn Thr Val Pro Ser
385                 390                 395                 400

Pro Ile Ile Gly Asp Gly Thr Asn Pro Thr Val Leu Leu Val Ser Val
                405                 410                 415

Ala Gly Ser Val Val Leu Val Val Ile Leu Ile Ala Ala Phe Val Ile
            420                 425                 430

Ser Arg Arg Arg Ser Lys Tyr Ser Lys Ala Lys Gln Glu Ala Asp Glu
        435                 440                 445

Glu Lys His Leu Asn Gln Gly Val Arg Thr Tyr Val Asp Pro Phe Thr
    450                 455                 460

Tyr Glu Asp Pro Asn Gln Ala Val Arg Glu Phe Ala Lys Glu Ile Asp
465                 470                 475                 480

Ala Ser Cys Ile Lys Ile Glu Lys Val Ile Gly Val Gly Glu Phe Gly
                485                 490                 495

Glu Val Cys Ser Gly Arg Leu Lys Val Pro Gly Lys Arg Glu Ile Cys
            500                 505                 510

Val Ala Ile Lys Thr Leu Lys Ala Gly Tyr Thr Asp Lys Gln Arg Arg
        515                 520                 525

Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro Asn
    530                 535                 540

Ile Ile His Leu Glu Gly Val Val Thr Lys Cys Lys Pro Val Met Ile
545                 550                 555                 560

Ile Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Ala Phe Leu Arg Lys
                565                 570                 575

Asn Asp Gly Arg Phe Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly
            580                 585                 590

Ile Gly Ser Gly Met Lys Tyr Leu Ser Asp Met Ser Tyr Val His Arg
        595                 600                 605

Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys
    610                 615                 620

Val Ser Asp Phe Gly Met Ser Arg Val Leu Glu Asp Asp Pro Glu Ala
625                 630                 635                 640

Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro
                645                 650                 655

Glu Ala Ile Ala Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser
            660                 665                 670

Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr
        675                 680                 685

Trp Asp Met Ser Asn Gln Asp Val Ile Lys Ala Ile Glu Glu Gly Tyr
    690                 695                 700

Arg Leu Pro Pro Pro Met Asp Cys Pro Ile Ala Leu His Gln Leu Met
705                 710                 715                 720
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Leu Asp Cys Trp Gln Lys Glu Arg Ser Asp Arg Pro Lys Phe Gly Gln
                725                 730                 735

Ile Val Asn Met Leu Asp Lys Leu Ile Arg Asn Pro Asn Ser Leu Lys
            740                 745                 750

Arg Thr Gly Ser Glu Ser Ser Arg Pro Ser Thr Ala Leu Leu Asp Pro
        755                 760                 765

Ser Ser Pro Glu Phe Ser Ala Val Val Ser Val Ser Asp Trp Leu Gln
    770                 775                 780

Ala Ile Lys Met Glu Arg Tyr Lys Asp Asn Phe Thr Ala Ala Gly Tyr
785                 790                 795                 800

Thr Thr Leu Glu Ala Val Val His Met Asn Gln Asp Asp Leu Ala Arg
                805                 810                 815

Ile Gly Ile Thr Ala Ile Thr His Gln Asn Lys Ile Leu Ser Ser Val
            820                 825                 830

Gln Ala Met Arg Ser Gln Met Gln Gln Met His Gly Arg Met Val Pro
        835                 840                 845

Val
```

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3776 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 290..3208

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

```
CGGCTCTGAC TTTGTGTTAA CGGTTTATGG ACTGGTTCCA AAGAGCTCAA AGGTACCAAA      60

ACACTCCAAG CAACCTCTGA ACCATTCAAG CAAGTAGTGT GTGTTTATTG GATATGGTGG     120

AGTCTACAGA GAATCTTCAT GGATTCTAAT GCTGACATCA GTGCAAGAAG AGTGTCAGGA     180

ATGGATTGGC TCTGGCTGGT TTGCTTCTTT CATCTAGTCA CTTCACTAGA AGACCTGCAT     240

CCTGACCAAC CGGAAAGGTG AGCAGGATGA GGCCATTGGT GGTGCTGTC ATG ACT         295
                                                      Met Thr
                                                        1

GAA ATA CTT CTG GAT ACA ACT GGA GAA ACC TCA GAG ATT GGC TGG ACC       343
Glu Ile Leu Leu Asp Thr Thr Gly Glu Thr Ser Glu Ile Gly Trp Thr
          5                  10                  15

TCT CAC CCT CCT GAT GGG TGG GAA GAA GTA AGT GTC CGG GAT GAT AAG       391
Ser His Pro Pro Asp Gly Trp Glu Glu Val Ser Val Arg Asp Asp Lys
     20                  25                  30

GAG CGC CAG ATC CGA ACC TTT CAA GTT TGT AAC ATG GAT GAA CCA GGT       439
Glu Arg Gln Ile Arg Thr Phe Gln Val Cys Asn Met Asp Glu Pro Gly
 35                  40                  45                  50
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CAG AAT AAC TGG TTG CGT ACT CAC TTC ATA GAG CGA CGT GGA GCC CAC        487
Gln Asn Asn Trp Leu Arg Thr His Phe Ile Glu Arg Arg Gly Ala His
                 55                  60                  65

CGA GTC CAT GTC CGC CTT CAT TTC TCA GTG AGG GAC TGT GCC AGC ATG        535
Arg Val His Val Arg Leu His Phe Ser Val Arg Asp Cys Ala Ser Met
             70                  75                  80

CGT ACT GTG GCC TCT ACT TGC AAA GAG ACT TTC ACA CTC TAC TAC CAC        583
Arg Thr Val Ala Ser Thr Cys Lys Glu Thr Phe Thr Leu Tyr Tyr His
         85                  90                  95

CAG TCA GAT GTC GAC ATA GCC TCT CAG GAA CTG CCA GAG TGG CAT GAA        631
Gln Ser Asp Val Asp Ile Ala Ser Gln Glu Leu Pro Glu Trp His Glu
     100                 105                 110

GGC CCC TGG ACC AAG GTG GAT ACT ATT GCA GCT GAT GAA AGC TTT TCC        679
Gly Pro Trp Thr Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser
115                 120                 125                 130

CAG GTG GAC AGA ACT GGG AAG GTG GTA AGG ATG AAT GTT AAA GTA CGC        727
Gln Val Asp Arg Thr Gly Lys Val Val Arg Met Asn Val Lys Val Arg
                 135                 140                 145

AGC TTT GGG CCA CTC ACA AAG CAT GGC TTC TAC CTG GCC TTC CAG GAC        775
Ser Phe Gly Pro Leu Thr Lys His Gly Phe Tyr Leu Ala Phe Gln Asp
             150                 155                 160

TCA GGA GCC TGT ATG TCC CTG GTG GCA GTC CAA GTC TTT TTC TAC AAG        823
Ser Gly Ala Cys Met Ser Leu Val Ala Val Gln Val Phe Phe Tyr Lys
         165                 170                 175

TGT CCA GCT GTG GTG AAA GGA TTT GCC TCC TTC CCT GAA ACT TTT GCT        871
Cys Pro Ala Val Val Lys Gly Phe Ala Ser Phe Pro Glu Thr Phe Ala
     180                 185                 190

GGA GGA GAG AGG ACC TCA CTG GTG GAG TCA CTA GGG ACG TGT GTA GCA        919
Gly Gly Glu Arg Thr Ser Leu Val Glu Ser Leu Gly Thr Cys Val Ala
195                 200                 205                 210

AAT GCT GAA GAG GCA AGC ACA ACT GGG TCA TCA GGT GTT CGG TTG CAC        967
Asn Ala Glu Glu Ala Ser Thr Thr Gly Ser Ser Gly Val Arg Leu His
                 215                 220                 225

TGC AAT GGA GAA GGA GAG TGG ATG GTG GCC ACT GGA CGA TGC TCT TGC       1015
Cys Asn Gly Glu Gly Glu Trp Met Val Ala Thr Gly Arg Cys Ser Cys
             230                 235                 240

AAG GCT GGT TAC CAA TCT GTT GAC AAT GAG CAA GCT TGT CAA GCT TGT       1063
Lys Ala Gly Tyr Gln Ser Val Asp Asn Glu Gln Ala Cys Gln Ala Cys
         245                 250                 255

CCC ATT GGT TCC TTT AAA GCA TCT GTG GGA GAT GAC CCT TGC CTT CTC       1111
Pro Ile Gly Ser Phe Lys Ala Ser Val Gly Asp Asp Pro Cys Leu Leu
     260                 265                 270

TGC CCT GCC CAC AGC CAT GCT CCA CTG CCA CTG CCA GGT TCC ATT GAA       1159
Cys Pro Ala His Ser His Ala Pro Leu Pro Leu Pro Gly Ser Ile Glu
275                 280                 285                 290

TGT GTG TGT CAG AGT CAC TAC TAC CGA TCT GCT TCT GAC AAT TCT GAT       1207
Cys Val Cys Gln Ser His Tyr Tyr Arg Ser Ala Ser Asp Asn Ser Asp
                 295                 300                 305

GCT CCC TGC ACT GGC ATC CCC TCT GCT CCC CGT GAC CTC AGT TAT GAA       1255
Ala Pro Cys Thr Gly Ile Pro Ser Ala Pro Arg Asp Leu Ser Tyr Glu
             310                 315                 320
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ATT GTT GGC TCC AAC GTG CTC CTG ACC TGG CGC CTC CCC AAG GAC TTG      1303
Ile Val Gly Ser Asn Val Leu Leu Thr Trp Arg Leu Pro Lys Asp Leu
        325                 330                 335

GGT GGC CGC AAG GAT GTC TTC TTC AAT GTC ATC TGC AAG GAA TGC CCA      1351
Gly Gly Arg Lys Asp Val Phe Phe Asn Val Ile Cys Lys Glu Cys Pro
    340                 345                 350

ACA AGG TCA GCA GGG ACA TGT GTG CGC TGT GGG GAC AAT GTA CAG TTT      1399
Thr Arg Ser Ala Gly Thr Cys Val Arg Cys Gly Asp Asn Val Gln Phe
355                 360                 365                 370

GAA CCA CGC CAA GTG GGC CTG ACA GAA AGT CGT GTT CAA GTC TCC AAC      1447
Glu Pro Arg Gln Val Gly Leu Thr Glu Ser Arg Val Gln Val Ser Asn
                375                 380                 385

CTA TTG GCC CGT GTG CAG TAC ACT TTT GAG ATC CAG GCT GTC AAT TTG      1495
Leu Leu Ala Arg Val Gln Tyr Thr Phe Glu Ile Gln Ala Val Asn Leu
            390                 395                 400

GTG ACT GAG TTG AGT TCA GAA GCA CCC CAG TAT GCT ACC ATC AAC GTT      1543
Val Thr Glu Leu Ser Ser Glu Ala Pro Gln Tyr Ala Thr Ile Asn Val
        405                 410                 415

AGC ACC AGC CAG TCA GTG CCC TCC GCA ATC CCT ATG ATG CAT CAG GTG      1591
Ser Thr Ser Gln Ser Val Pro Ser Ala Ile Pro Met Met His Gln Val
    420                 425                 430

AGT CGT GCT ACC AGT AGC ATC ACA CTG TCT TGG CCT CAG CCA GAC CAG      1639
Ser Arg Ala Thr Ser Ser Ile Thr Leu Ser Trp Pro Gln Pro Asp Gln
435                 440                 445                 450

CCC AAT GGG GTT ATC CTG GAT TAC CAG CTA CGG TAC TTT GAC AAG GCA      1687
Pro Asn Gly Val Ile Leu Asp Tyr Gln Leu Arg Tyr Phe Asp Lys Ala
                455                 460                 465

GAA GAT GAG GAT AAT TCA TTT ACT TTG ACT AGT GAA ACT AAC ATG GCC      1735
Glu Asp Glu Asp Asn Ser Phe Thr Leu Thr Ser Glu Thr Asn Met Ala
            470                 475                 480

ACT ATA TTA AAT CTG AGT CCA GGC AAG ATC TAT GTC TTC CAA GTA CGA      1783
Thr Ile Leu Asn Leu Ser Pro Gly Lys Ile Tyr Val Phe Gln Val Arg
        485                 490                 495

GCT AGA ACA GCA GTG GGT TAT GGC CCA TAC AGT GGA AAG ATG TAT TTC      1831
Ala Arg Thr Ala Val Gly Tyr Gly Pro Tyr Ser Gly Lys Met Tyr Phe
    500                 505                 510

CAG ACT TTA ATG GCA GGA GAG CAC TCG GAG ATG GCA CAG GAC CGA CTG      1879
Gln Thr Leu Met Ala Gly Glu His Ser Glu Met Ala Gln Asp Arg Leu
515                 520                 525                 530

CCA CTT ATT GTG GGC TCA GCA CTT GGT GGT CTG GCA TTC TTG GTA ATT      1927
Pro Leu Ile Val Gly Ser Ala Leu Gly Gly Leu Ala Phe Leu Val Ile
                535                 540                 545

GCT GCC ATT GCC ATT CTT GCC ATC ATC TTC AAG AGT AAA AGG CGA GAG      1975
Ala Ala Ile Ala Ile Leu Ala Ile Ile Phe Lys Ser Lys Arg Arg Glu
            550                 555                 560

ACT CCA TAC ACA GAC CGC CTG CAG CAG TAT ATC AGT ACA CGA GGA CTT      2023
Thr Pro Tyr Thr Asp Arg Leu Gln Gln Tyr Ile Ser Thr Arg Gly Leu
        565                 570                 575

GGA GTG AAG TAT TAC ATT GAT CCT TCC ACG TAT GAA GAT CCC AAT GAA      2071
Gly Val Lys Tyr Tyr Ile Asp Pro Ser Thr Tyr Glu Asp Pro Asn Glu
    580                 585                 590
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GCT ATT CGA GAG TTT GCC AAA GAG ATA GAT GTG TCC TTC ATC AAA ATT      2119
Ala Ile Arg Glu Phe Ala Lys Glu Ile Asp Val Ser Phe Ile Lys Ile
595                 600                 605                 610

GAG GAG GTC ATT GGA TCA GGA GAA TTT GGA GAG GTG TGC TTT GGG CGC      2167
Glu Glu Val Ile Gly Ser Gly Glu Phe Gly Glu Val Cys Phe Gly Arg
                615                 620                 625

CTA AAA CAC CCA GGG AAA CGT GAA TAC ACA GTA GCT ATT AAA ACC CTG      2215
Leu Lys His Pro Gly Lys Arg Glu Tyr Thr Val Ala Ile Lys Thr Leu
            630                 635                 640

AAG TCA GGT TAT ACT GAT GAA CAG CGT CGA GAG TTC CTG AGC GAG GCC      2263
Lys Ser Gly Tyr Thr Asp Glu Gln Arg Arg Glu Phe Leu Ser Glu Ala
        645                 650                 655

AGC ATC ATG GGG CAA TTT GAG CAT CCC AAT GTC ATC CAC CTG GAG GGC      2311
Ser Ile Met Gly Gln Phe Glu His Pro Asn Val Ile His Leu Glu Gly
    660                 665                 670

GTG GTC ACC AAA AGC CGA CCA GTC ATG ATT GTC ACA GAA TTC ATG GAG      2359
Val Val Thr Lys Ser Arg Pro Val Met Ile Val Thr Glu Phe Met Glu
675                 680                 685                 690

AAT GGA TCA CTG GAT TCC TTC CTC AGG GAG AAG GAG GGA CAG TTC AGT      2407
Asn Gly Ser Leu Asp Ser Phe Leu Arg Glu Lys Glu Gly Gln Phe Ser
                695                 700                 705

GTG TTA CAG CTG GTG GGA ATG CTA CGA GGG ATT GCA GCA GGC ATG CGC      2455
Val Leu Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met Arg
            710                 715                 720

TAC CTT TCA GAC ATG AAC TAT GTG CAT CGT GAT CTC GCA GCA CGT AAC      2503
Tyr Leu Ser Asp Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn
        725                 730                 735

ATC TTA GTC AAC AGT AAC CTT GTA TGC AAG GTG TCA GAC TTT GGT TTG      2551
Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu
    740                 745                 750

TCT CGC TTT CTG GAA GAT GAT GCT TCA AAT CCC ACT TAT ACT GGA GCT      2599
Ser Arg Phe Leu Glu Asp Asp Ala Ser Asn Pro Thr Tyr Thr Gly Ala
755                 760                 765                 770

CTG GGT TGC AAA ATC CCC ATC CGT TGG ACT GCC CCT GAA GCT GTC CAG      2647
Leu Gly Cys Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Val Gln
                775                 780                 785

TAT CGC AAG TTC ACC TCC TCC AGT GAT GTC TGG AGC TAT GGC ATT GTC      2695
Tyr Arg Lys Phe Thr Ser Ser Ser Asp Val Trp Ser Tyr Gly Ile Val
            790                 795                 800

ATG TGG GAG GTG ATG TCC TAT GGT GAG AGA CCT TAC TGG GAC ATG TCC      2743
Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Ser
        805                 810                 815

AAC CAG GAT GTA ATT AAT GCC ATT GAC CAG GAC TAT CGC CTG CCA CCA      2791
Asn Gln Asp Val Ile Asn Ala Ile Asp Gln Asp Tyr Arg Leu Pro Pro
    820                 825                 830

CCC CCA GAC TGC CCA ACT GTT TTG CAT CTG CTG ATG CTT GAC TGC TGG      2839
Pro Pro Asp Cys Pro Thr Val Leu His Leu Leu Met Leu Asp Cys Trp
835                 840                 845                 850

CAG AAG GAT CGA GTC CAG AGA CCA AAA TTT GAA CAA ATA GTC AGT GCC      2887
Gln Lys Asp Arg Val Gln Arg Pro Lys Phe Glu Gln Ile Val Ser Ala
                855                 860                 865
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CTA GAT AAA ATG ATC CGC AAG CCA TCT GCT CTC AAA GCC ACT GGC ACT      2935
Leu Asp Lys Met Ile Arg Lys Pro Ser Ala Leu Lys Ala Thr Gly Thr
            870                 875                 880

GGG AGC AGC AGA CCA TCT CAG CCT CTC CTG AGC AAC TCC CCT CCA GAT      2983
Gly Ser Ser Arg Pro Ser Gln Pro Leu Leu Ser Asn Ser Pro Pro Asp
        885                 890                 895

TTT CCT TCA CTC AGC AAT GCC CAC GAG TGG TTG GAT GCC ATC AAG ATG      3031
Phe Pro Ser Leu Ser Asn Ala His Glu Trp Leu Asp Ala Ile Lys Met
    900                 905                 910

GGT CGT TAC AAG GAG AAT TTT GAC CAG GCT GGT CTG ATT ACA TTT GAT      3079
Gly Arg Tyr Lys Glu Asn Phe Asp Gln Ala Gly Leu Ile Thr Phe Asp
915                 920                 925                 930

GTC ATA TCA CGC ATG ACT CTG GAA GAT CTC CAG CGT ATT GGA ATC ACC      3127
Val Ile Ser Arg Met Thr Leu Glu Asp Leu Gln Arg Ile Gly Ile Thr
                935                 940                 945

CTG GTT GGT CAC CAG AAA AAG ATT CTA AAC AGC ATC CAG CTC ATG AAA      3175
Leu Val Gly His Gln Lys Lys Ile Leu Asn Ser Ile Gln Leu Met Lys
            950                 955                 960

GTT CAT TTG AAC CAG CTT GAA CCA GTT GAA GTG TGATGCTTTA AGTCTCTATT    3228
Val His Leu Asn Gln Leu Glu Pro Val Glu Val
        965                 970

TCACCAGACT CAAATTCTGA AAGAGTCCTG AGGGGATTCA GAGGGATTGT CACTGTATGA    3288

AAAGGAAATG GCAAGATGCT CCTTGAAGAC TTACTGCACC TAGAGAGTAG ACATTACACA    3348

TTCCATTCCA CCAGCAAAAA GAGAATCTTG CCATCATTTA AAAGCAGAGT TAAATAGCTG    3408

GTGGTTAAAT ATGACTGGCA TCATACACTA GGAGTAGGTC AGGGAGGGAA AGTTATAGTA    3468

ATGCAGAGTG GAGCTGGTAT AATAGTTTGG ACAGACCACA AGCACCTGCT AGCTCTTCTC    3528

CACTAAATAA AAAATCAGAC AATTCTCCAG TGCCATCAGC AGGCTTTATC TGTGACTGGG    3588

AACAAAGAAA TCACAATTTT TCCAAGAGAG TATCAGCACA TTGTGAGAGT TATCACTCAG    3648

TTGGAAATGG ACATCACTTG CTATGCCAGA TTTGTGAGAA ACTGGAGTTC CACTGAGTGC    3708

ACCATATGTG GTAAACAATA AGGTACATCA CCTCGTAATT TTTACAGAGG TTGAGAGTAA    3768

AGGGCCCA                                                             3776
```

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 973 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

```
Met Thr Glu Ile Leu Leu Asp Thr Thr Gly Glu Thr Ser Glu Ile Gly
 1               5                  10                  15

Trp Thr Ser His Pro Pro Asp Gly Trp Glu Glu Val Ser Val Arg Asp
            20                  25                  30
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Asp Lys Glu Arg Gln Ile Arg Thr Phe Gln Val Cys Asn Met Asp Glu
         35                  40                  45

Pro Gly Gln Asn Asn Trp Leu Arg Thr His Phe Ile Glu Arg Arg Gly
     50                  55                  60

Ala His Arg Val His Val Arg Leu His Phe Ser Val Arg Asp Cys Ala
 65                  70                  75                  80

Ser Met Arg Thr Val Ala Ser Thr Cys Lys Glu Thr Phe Thr Leu Tyr
                 85                  90                  95

Tyr His Gln Ser Asp Val Asp Ile Ala Ser Gln Glu Leu Pro Glu Trp
            100                 105                 110

His Glu Gly Pro Trp Thr Lys Val Asp Thr Ile Ala Ala Asp Glu Ser
        115                 120                 125

Phe Ser Gln Val Asp Arg Thr Gly Lys Val Val Arg Met Asn Val Lys
    130                 135                 140

Val Arg Ser Phe Gly Pro Leu Thr Lys His Gly Phe Tyr Leu Ala Phe
145                 150                 155                 160

Gln Asp Ser Gly Ala Cys Met Ser Leu Val Ala Val Gln Val Phe Phe
                165                 170                 175

Tyr Lys Cys Pro Ala Val Val Lys Gly Phe Ala Ser Phe Pro Glu Thr
            180                 185                 190

Phe Ala Gly Gly Glu Arg Thr Ser Leu Val Glu Ser Leu Gly Thr Cys
        195                 200                 205

Val Ala Asn Ala Glu Glu Ala Ser Thr Thr Gly Ser Ser Gly Val Arg
    210                 215                 220

Leu His Cys Asn Gly Glu Gly Glu Trp Met Val Ala Thr Gly Arg Cys
225                 230                 235                 240

Ser Cys Lys Ala Gly Tyr Gln Ser Val Asp Asn Glu Gln Ala Cys Gln
                245                 250                 255

Ala Cys Pro Ile Gly Ser Phe Lys Ala Ser Val Gly Asp Asp Pro Cys
            260                 265                 270

Leu Leu Cys Pro Ala His Ser His Ala Pro Leu Pro Leu Pro Gly Ser
        275                 280                 285

Ile Glu Cys Val Cys Gln Ser His Tyr Tyr Arg Ser Ala Ser Asp Asn
    290                 295                 300

Ser Asp Ala Pro Cys Thr Gly Ile Pro Ser Ala Pro Arg Asp Leu Ser
305                 310                 315                 320

Tyr Glu Ile Val Gly Ser Asn Val Leu Leu Thr Trp Arg Leu Pro Lys
                325                 330                 335

Asp Leu Gly Gly Arg Lys Asp Val Phe Phe Asn Val Ile Cys Lys Glu
            340                 345                 350

Cys Pro Thr Arg Ser Ala Gly Thr Cys Val Arg Cys Gly Asp Asn Val
        355                 360                 365

Gln Phe Glu Pro Arg Gln Val Gly Leu Thr Glu Ser Arg Val Gln Val
    370                 375                 380
```

Ser Asn Leu Leu Ala Arg Val Gln Tyr Thr Phe Glu Ile Gln Ala Val
385 390 395 400

Asn Leu Val Thr Glu Leu Ser Ser Glu Ala Pro Gln Tyr Ala Thr Ile
405 410 415

Asn Val Ser Thr Ser Gln Ser Val Pro Ser Ala Ile Pro Met Met His
420 425 430

Gln Val Ser Arg Ala Thr Ser Ser Ile Thr Leu Ser Trp Pro Gln Pro
435 440 445

Asp Gln Pro Asn Gly Val Ile Leu Asp Tyr Gln Leu Arg Tyr Phe Asp
450 455 460

Lys Ala Glu Asp Glu Asp Asn Ser Phe Thr Leu Thr Ser Glu Thr Asn
465 470 475 480

Met Ala Thr Ile Leu Asn Leu Ser Pro Gly Lys Ile Tyr Val Phe Gln
485 490 495

Val Arg Ala Arg Thr Ala Val Gly Tyr Gly Pro Tyr Ser Gly Lys Met
500 505 510

Tyr Phe Gln Thr Leu Met Ala Gly Glu His Ser Glu Met Ala Gln Asp
515 520 525

Arg Leu Pro Leu Ile Val Gly Ser Ala Leu Gly Gly Leu Ala Phe Leu
530 535 540

Val Ile Ala Ala Ile Ala Ile Leu Ala Ile Ile Phe Lys Ser Lys Arg
545 550 555 560

Arg Glu Thr Pro Tyr Thr Asp Arg Leu Gln Gln Tyr Ile Ser Thr Arg
565 570 575

Gly Leu Gly Val Lys Tyr Tyr Ile Asp Pro Ser Thr Tyr Glu Asp Pro
580 585 590

Asn Glu Ala Ile Arg Glu Phe Ala Lys Glu Ile Asp Val Ser Phe Ile
595 600 605

Lys Ile Glu Glu Val Ile Gly Ser Gly Glu Phe Gly Glu Val Cys Phe
610 615 620

Gly Arg Leu Lys His Pro Gly Lys Arg Glu Tyr Thr Val Ala Ile Lys
625 630 635 640

Thr Leu Lys Ser Gly Tyr Thr Asp Glu Gln Arg Arg Glu Phe Leu Ser
645 650 655

Glu Ala Ser Ile Met Gly Gln Phe Glu His Pro Asn Val Ile His Leu
660 665 670

Glu Gly Val Val Thr Lys Ser Arg Pro Val Met Ile Val Thr Glu Phe
675 680 685

Met Glu Asn Gly Ser Leu Asp Ser Phe Leu Arg Glu Lys Glu Gly Gln
690 695 700

Phe Ser Val Leu Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly
705 710 715 720

Met Arg Tyr Leu Ser Asp Met Asn Tyr Val His Arg Asp Leu Ala Ala
725 730 735

```
Arg Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe
            740                 745                 750

Gly Leu Ser Arg Phe Leu Glu Asp Asp Ala Ser Asn Pro Thr Tyr Thr
        755                 760                 765

Gly Ala Leu Gly Cys Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala
    770                 775                 780

Val Gln Tyr Arg Lys Phe Thr Ser Ser Ser Asp Val Trp Ser Tyr Gly
785                 790                 795                 800

Ile Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp
                805                 810                 815

Met Ser Asn Gln Asp Val Ile Asn Ala Ile Asp Gln Asp Tyr Arg Leu
            820                 825                 830

Pro Pro Pro Pro Asp Cys Pro Thr Val Leu His Leu Leu Met Leu Asp
        835                 840                 845

Cys Trp Gln Lys Asp Arg Val Gln Arg Pro Lys Phe Glu Gln Ile Val
    850                 855                 860

Ser Ala Leu Asp Lys Met Ile Arg Lys Pro Ser Ala Leu Lys Ala Thr
865                 870                 875                 880

Gly Thr Gly Ser Ser Arg Pro Ser Gln Pro Leu Leu Ser Asn Ser Pro
                885                 890                 895

Pro Asp Phe Pro Ser Leu Ser Asn Ala His Glu Trp Leu Asp Ala Ile
            900                 905                 910

Lys Met Gly Arg Tyr Lys Glu Asn Phe Asp Gln Ala Gly Leu Ile Thr
        915                 920                 925

Phe Asp Val Ile Ser Arg Met Thr Leu Glu Asp Leu Gln Arg Ile Gly
    930                 935                 940

Ile Thr Leu Val Gly His Gln Lys Lys Ile Leu Asn Ser Ile Gln Leu
945                 950                 955                 960

Met Lys Val His Leu Asn Gln Leu Glu Pro Val Glu Val
                965                 970
```

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3546 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..2920

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

```
C GGG GTC TCC TCG AGG GCG CGG CGG CCG CCG GGC AGC AGC AGG AGC          46
  Gly Val Ser Ser Arg Ala Arg Arg Pro Pro Gly Ser Ser Arg Ser
    1               5                  10                  15
```

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AGC AGG AGG GGG GTG ACC TCG GAG CTG GCA TGG ACA ACC CAT CCG GAG          94
Ser Arg Arg Gly Val Thr Ser Glu Leu Ala Trp Thr Thr His Pro Glu
                20                  25                  30

ACG GGG TGG GAA GAG GTC AGT GGT TAC GAC GAG GCT ATG AAC CCC ATC         142
Thr Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Ala Met Asn Pro Ile
            35                  40                  45

CGC ACA TAC CAG GTG TGC AAC GTG CGG GAG GCC AAC CAG AAC AAC TGG         190
Arg Thr Tyr Gln Val Cys Asn Val Arg Glu Ala Asn Gln Asn Asn Trp
        50                  55                  60

CTT CGC ACC AAG TTC ATT CAG CGC CAG GAC GTC CAG CGT GTC TAC GTG         238
Leu Arg Thr Lys Phe Ile Gln Arg Gln Asp Val Gln Arg Val Tyr Val
    65                  70                  75

GAG CTG AAA TTC ACT GTG CGG GAC TGC AAC AGC ATC CCC AAC ATC CCT         286
Glu Leu Lys Phe Thr Val Arg Asp Cys Asn Ser Ile Pro Asn Ile Pro
80                  85                  90                  95

GGT TCC TGC AAA GAG ACC TTC AAC CTC TTC TAT TAT GAG TCA GAT ACG         334
Gly Ser Cys Lys Glu Thr Phe Asn Leu Phe Tyr Tyr Glu Ser Asp Thr
                100                 105                 110

GAT TCT GCC TCT GCC AAT AGC CCT TTC TGG ATG GAG AAC CCC TAT ATC         382
Asp Ser Ala Ser Ala Asn Ser Pro Phe Trp Met Glu Asn Pro Tyr Ile
            115                 120                 125

AAA GTG GAT ACA ATT GCT CCG GAT GAG AGC TTC TCC AAA CTG GAG TCC         430
Lys Val Asp Thr Ile Ala Pro Asp Glu Ser Phe Ser Lys Leu Glu Ser
        130                 135                 140

GGC CGT GTG AAC ACC AAG GTG CGC AGC TTT GGG CCG CTC TCC AAG AAT         478
Gly Arg Val Asn Thr Lys Val Arg Ser Phe Gly Pro Leu Ser Lys Asn
    145                 150                 155

GGC TTT TAT CTG GCT TTC CAG GAC CTG GGG GCC TGC ATG TCC CTT ATC         526
Gly Phe Tyr Leu Ala Phe Gln Asp Leu Gly Ala Cys Met Ser Leu Ile
160                 165                 170                 175

TCC GTC CGG GCT TTC TAC AAG AAA TGT TCC AAC ACC ATC GCT GGC TTT         574
Ser Val Arg Ala Phe Tyr Lys Lys Cys Ser Asn Thr Ile Ala Gly Phe
                180                 185                 190

GCT ATC TTC CCG GAG ACC CTA ACG GGG GCT GAG CCC ACG TCG CTG GTC         622
Ala Ile Phe Pro Glu Thr Leu Thr Gly Ala Glu Pro Thr Ser Leu Val
            195                 200                 205

ATT GCG CCG GGC ACC TGC ATC CCC AAC GCA GTG GAA GTG TCT GTG CCC         670
Ile Ala Pro Gly Thr Cys Ile Pro Asn Ala Val Glu Val Ser Val Pro
        210                 215                 220

CTG AAG CTG TAC TGC AAC GGT GAT GGC GAG TGG ATG GTG CCT GTG GGA         718
Leu Lys Leu Tyr Cys Asn Gly Asp Gly Glu Trp Met Val Pro Val Gly
    225                 230                 235

GCG TGC ACG TGT GCT GCT GGG TAC GAG CCA GCC ATG AAG GAT ACC CAG         766
Ala Cys Thr Cys Ala Ala Gly Tyr Glu Pro Ala Met Lys Asp Thr Gln
240                 245                 250                 255

TGC CAA GCA TGC GGC CCG GGG ACG TTC AAA TCC AAG CAG GGC GAG GGC         814
Cys Gln Ala Cys Gly Pro Gly Thr Phe Lys Ser Lys Gln Gly Glu Gly
                260                 265                 270

CCC TGC TCC CCC TGC CCT CCC AAC AGC CGC ACC ACC GCG GGG GCA GCC         862
Pro Cys Ser Pro Cys Pro Pro Asn Ser Arg Thr Thr Ala Gly Ala Ala
            275                 280                 285
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ACA GTC TGC ATA TGT CGC AGC GGC TTC TTC CGA GCA GAC GCG GAC CCC        910
Thr Val Cys Ile Cys Arg Ser Gly Phe Phe Arg Ala Asp Ala Asp Pro
        290                 295                 300

GCA GAC AGC GCC TGC ACC AGT GTG CCC TCA GCC CCA CGC AGC GTC ATC        958
Ala Asp Ser Ala Cys Thr Ser Val Pro Ser Ala Pro Arg Ser Val Ile
    305                 310                 315

TCC AAC GTG AAT GAG ACG TCG TTG GTG CTG GAG TGG AGC GAG CCG CAG       1006
Ser Asn Val Asn Glu Thr Ser Leu Val Leu Glu Trp Ser Glu Pro Gln
320                 325                 330                 335

GAC GCG GGC GGG CGG GAT GAC CTG CTC TAC AAC GTC ATC TGC AAG AAG       1054
Asp Ala Gly Gly Arg Asp Asp Leu Leu Tyr Asn Val Ile Cys Lys Lys
                340                 345                 350

TGC AGC GTG GAG CGG CGG CTG TGC AGC CGC TGC GAC GAC AAC GTG GAG       1102
Cys Ser Val Glu Arg Arg Leu Cys Ser Arg Cys Asp Asp Asn Val Glu
            355                 360                 365

TTC GTG CCG CGC CAG CTG GGC CTC ACT GGC CTC ACT GAG CGA CGC ATC       1150
Phe Val Pro Arg Gln Leu Gly Leu Thr Gly Leu Thr Glu Arg Arg Ile
        370                 375                 380

TAC ATC AGC AAG GTG ATG GCC CAC CCC CAG TAC ACC TTC GAG ATC CAG       1198
Tyr Ile Ser Lys Val Met Ala His Pro Gln Tyr Thr Phe Glu Ile Gln
    385                 390                 395

GCG GTG AAT GGC ATC TCC AGC AAG AGC CCC TAC CCT CCC CAT TTT GCC       1246
Ala Val Asn Gly Ile Ser Ser Lys Ser Pro Tyr Pro Pro His Phe Ala
400                 405                 410                 415

TCC GTC AAC ATC ACG ACC AAC CAG GCA GCC CCA TCT GCC GTG CCC ACC       1294
Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Ala Val Pro Thr
                420                 425                 430

ATG CAT CTG CAC AGC AGC ACC GGG AAC AGC ATG ACA CTG TCA TGG ACT       1342
Met His Leu His Ser Ser Thr Gly Asn Ser Met Thr Leu Ser Trp Thr
            435                 440                 445

CCC CCG GAA AGG CCC AAC GGC ATC ATT CTC GAC TAT GAA ATC AAG TAC       1390
Pro Pro Glu Arg Pro Asn Gly Ile Ile Leu Asp Tyr Glu Ile Lys Tyr
        450                 455                 460

TCC GAG AAG CAA GGC CAG GGT GAC GGC ATT GCC AAC ACT GTC ACC AGC       1438
Ser Glu Lys Gln Gly Gln Gly Asp Gly Ile Ala Asn Thr Val Thr Ser
    465                 470                 475

CAG AAG AAC TCG GTG CGG CTG GAC GGA CTG AAG GCC AAT GCT CGG TAC       1486
Gln Lys Asn Ser Val Arg Leu Asp Gly Leu Lys Ala Asn Ala Arg Tyr
480                 485                 490                 495

ATG GTG CAG GTC CGG GCG CGC ACA GTG GCT GGA TAC GGC CGC TAC AGC       1534
Met Val Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly Arg Tyr Ser
                500                 505                 510

CTC CCC ACC GAG TTC CAG ACG ACT GCG GAG GAT GGC TCC ACC AGC AAG       1582
Leu Pro Thr Glu Phe Gln Thr Thr Ala Glu Asp Gly Ser Thr Ser Lys
            515                 520                 525

ACT TTC CAG GAG CTT CCT CTC ATC GTG GGT TCA GCC ACC GCG GGA CTG       1630
Thr Phe Gln Glu Leu Pro Leu Ile Val Gly Ser Ala Thr Ala Gly Leu
        530                 535                 540

CTG TTT GTC ATC GTG GTG GTC ATC ATC GCT ATT GTC TGC TTC AGG AAG       1678
Leu Phe Val Ile Val Val Val Ile Ile Ala Ile Val Cys Phe Arg Lys
    545                 550                 555
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CAG CGC AAC AGC ACA GAT CCC GAG TAC ACA GAG AAG CTG CAG CAA TAT      1726
Gln Arg Asn Ser Thr Asp Pro Glu Tyr Thr Glu Lys Leu Gln Gln Tyr
560                 565                 570                 575

GTC ACT CCT GGG ATG AAG GTC TAC ATT GAC CCC TTC ACC TAT GAA GAC      1774
Val Thr Pro Gly Met Lys Val Tyr Ile Asp Pro Phe Thr Tyr Glu Asp
                580                 585                 590

CCA AAT GAA GCT GTC CGG GAA TTC GCC AAA GAG ATT GAT ATC TCC TGT      1822
Pro Asn Glu Ala Val Arg Glu Phe Ala Lys Glu Ile Asp Ile Ser Cys
            595                 600                 605

GTC AAA ATT GAG GAG GTC ATT GGA GCA GGA GAG TTT GGT GAG GTG TGC      1870
Val Lys Ile Glu Glu Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys
        610                 615                 620

CGT GGG CGC CTG AAG CTG CCT GGC CGC CGT GAG ATC TTT GTG GCC ATC      1918
Arg Gly Arg Leu Lys Leu Pro Gly Arg Arg Glu Ile Phe Val Ala Ile
    625                 630                 635

AAG ACA CTG AAG GTG GGC TAC ACA GAG AGG CAG CGG CGG GAC TTC CTG      1966
Lys Thr Leu Lys Val Gly Tyr Thr Glu Arg Gln Arg Arg Asp Phe Leu
640                 645                 650                 655

AGT GAG GCC AGC ATC ATG GGC CAG TTC GAC CAC CCC AAC ATC ATC CAC      2014
Ser Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His
                660                 665                 670

CTG GAG GGC GTG GTG ACC AAG AGC CGC CCT GTC ATG ATC ATC ACA GAG      2062
Leu Glu Gly Val Val Thr Lys Ser Arg Pro Val Met Ile Ile Thr Glu
            675                 680                 685

TTC ATG GAG AAC TGC GCT CTC GAC TCC TTC CTC CGG CTG AAT GAT GGG      2110
Phe Met Glu Asn Cys Ala Leu Asp Ser Phe Leu Arg Leu Asn Asp Gly
        690                 695                 700

CAG TTC ACG GTC ATC CAG CTG GTG GGG ATG CTG CGA GGC ATC GCT GCT      2158
Gln Phe Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala
    705                 710                 715

GGC ATG AAG TAC CTC TCA GAG ATG AAC TAC GTG CAC CGA GAC CTG GCT      2206
Gly Met Lys Tyr Leu Ser Glu Met Asn Tyr Val His Arg Asp Leu Ala
720                 725                 730                 735

GCC CGC AAC ATC CTG GTC AAC AGC AAC TTG GTC TGC AAA GTG TCT GAC      2254
Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp
                740                 745                 750

TTC GGG CTC TCC CGC TTT TTG GAG GAT GAT CCA GCC GAC CCC ACC TAC      2302
Phe Gly Leu Ser Arg Phe Leu Glu Asp Asp Pro Ala Asp Pro Thr Tyr
            755                 760                 765

ACC AGC TCC CTG GGA GGC AAG ATC CCC ATC AGG TGG ACA GCT CCT GAG      2350
Thr Ser Ser Leu Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu
        770                 775                 780

GCC ATC GCC TAC CGC AAA TTC ACG TCG GCC AGC GAC GTG TGG AGC TAC      2398
Ala Ile Ala Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr
    785                 790                 795

GGC ATC GTC ATG TGG GAA GTG ATG TCC TAC GGG GAG CGA CCC TAC TGG      2446
Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp
800                 805                 810                 815

GAC ATG TCC AAC CAG GAT GTG ATC AAC GCG GTG GAG CAG GAT TAC CGC      2494
Asp Met Ser Asn Gln Asp Val Ile Asn Ala Val Glu Gln Asp Tyr Arg
                820                 825                 830
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CTG CCA CCC CCC ATG GAC TGC CCC ACA GCA CTG CAC CAG CTG ATG CTG      2542
Leu Pro Pro Pro Met Asp Cys Pro Thr Ala Leu His Gln Leu Met Leu
            835                 840                 845

GAC TGC TGG GTG CGG GAC CGC AAC CTG CGG CCC AAG TTT GCA CAG ATT      2590
Asp Cys Trp Val Arg Asp Arg Asn Leu Arg Pro Lys Phe Ala Gln Ile
        850                 855                 860

GTC AAC ACG CTG GAC AAG CTG ATC CGC AAT GCT GCC AGC CTG AAG GTC      2638
Val Asn Thr Leu Asp Lys Leu Ile Arg Asn Ala Ala Ser Leu Lys Val
    865                 870                 875

ATC GCC AGC GTC CAG TCC GGT GTC TCC CAG CCG CTC CTG GAC CGC ACC      2686
Ile Ala Ser Val Gln Ser Gly Val Ser Gln Pro Leu Leu Asp Arg Thr
880                 885                 890                 895

GTG CCC GAT TAC ACC ACC TTC ACC ACC GTG GGA GAC TGG CTG GAT GCC      2734
Val Pro Asp Tyr Thr Thr Phe Thr Thr Val Gly Asp Trp Leu Asp Ala
                900                 905                 910

ATC AAA ATG GGA CGG TAC AAG GAG AAC TTC GTC AAC GCC GGC TTC GCC      2782
Ile Lys Met Gly Arg Tyr Lys Glu Asn Phe Val Asn Ala Gly Phe Ala
            915                 920                 925

TCC TTT GAC CTG GTG GCA CAG ATG ACA GCA GAG GAC CTG CTA AGG ATA      2830
Ser Phe Asp Leu Val Ala Gln Met Thr Ala Glu Asp Leu Leu Arg Ile
        930                 935                 940

GGA GTG ACG CTA GCA GGG CAC CAG AAG AAG ATC CTG AGC AGC ATT CAG      2878
Gly Val Thr Leu Ala Gly His Gln Lys Lys Ile Leu Ser Ser Ile Gln
    945                 950                 955

GAC ATG AGG CTG CAG ATG AAC CAG ACG CTG CCG GTT CAG GTT              2920
Asp Met Arg Leu Gln Met Asn Gln Thr Leu Pro Val Gln Val
960                 965                 970

TGACCGCAGG GACTCTGCAT TGGAACGGAC TGAGGGAACC TGCCAACCAG GTTCTGTTTG    2980

CGGTGCAGCC CGGCTTCCCG ATTTCCCCTT CCCGTGGCGC TCCTCTGCCT CGGACGCTCG    3040

CCGGGGACAG GCTGGGCCGG GCCACCCTTC CCTGGATCAG AGGCACTCGT GCCGGGAGGG    3100

AGCCCGGCTT TTCGTCCCGT GTCCCGCAGC GGCGAGGCAG TGAACGCAGT CTTCATATTG    3160

AAGATGGATT ATGGGACGGA GATGGCGCAT CCGCTTCCCG CCCTGTCTCA GTGCTCATCA    3220

GTTTGAAGAG ATGTTCTGCT TCTTGGATTT CTTTACACCC CGGTTTTCCC CCCTCGAGTC    3280

CTCACTTCCC CCTATCCCTG AGGCCACAGA CTGTTGACCC GTCCGCTGAG TCCGTCAGAC    3340

GCTCCGAAGC CTTCCCCGAG CCCGGTCCCC GCGTGGAGAC GGCGCCAGGG ACGGGGCTAC    3400

GGCCCCAGAC AATCACTCCA CCCCTCCGCA CGAGGGTCCT CACTGGGACG TGTCTGAAGG    3460

GGAAAGGCTC TGCTCCCTTT TTGGCTTTGC ACGCCAGAAC CCGAACCCCG TGAGATTTAC    3520

TATGCAGGGA GTTAGGCAAA AAAAAG                                         3546
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(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 973 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

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Gly Val Ser Ser Arg Ala Arg Arg Pro Pro Gly Ser Ser Arg Ser Ser
 1               5                  10                  15

Arg Arg Gly Val Thr Ser Glu Leu Ala Trp Thr Thr His Pro Glu Thr
            20                  25                  30

Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Ala Met Asn Pro Ile Arg
        35                  40                  45

Thr Tyr Gln Val Cys Asn Val Arg Glu Ala Asn Gln Asn Asn Trp Leu
    50                  55                  60

Arg Thr Lys Phe Ile Gln Arg Gln Asp Val Gln Arg Val Tyr Val Glu
65                  70                  75                  80

Leu Lys Phe Thr Val Arg Asp Cys Asn Ser Ile Pro Asn Ile Pro Gly
                85                  90                  95

Ser Cys Lys Glu Thr Phe Asn Leu Phe Tyr Tyr Glu Ser Asp Thr Asp
            100                 105                 110

Ser Ala Ser Ala Asn Ser Pro Phe Trp Met Glu Asn Pro Tyr Ile Lys
        115                 120                 125

Val Asp Thr Ile Ala Pro Asp Glu Ser Phe Ser Lys Leu Glu Ser Gly
    130                 135                 140

Arg Val Asn Thr Lys Val Arg Ser Phe Gly Pro Leu Ser Lys Asn Gly
145                 150                 155                 160

Phe Tyr Leu Ala Phe Gln Asp Leu Gly Ala Cys Met Ser Leu Ile Ser
                165                 170                 175

Val Arg Ala Phe Tyr Lys Lys Cys Ser Asn Thr Ile Ala Gly Phe Ala
            180                 185                 190

Ile Phe Pro Glu Thr Leu Thr Gly Ala Glu Pro Thr Ser Leu Val Ile
        195                 200                 205

Ala Pro Gly Thr Cys Ile Pro Asn Ala Val Glu Val Ser Val Pro Leu
    210                 215                 220

Lys Leu Tyr Cys Asn Gly Asp Gly Glu Trp Met Val Pro Val Gly Ala
225                 230                 235                 240

Cys Thr Cys Ala Ala Gly Tyr Glu Pro Ala Met Lys Asp Thr Gln Cys
                245                 250                 255

Gln Ala Cys Gly Pro Gly Thr Phe Lys Ser Lys Gln Gly Glu Gly Pro
            260                 265                 270

Cys Ser Pro Cys Pro Pro Asn Ser Arg Thr Thr Ala Gly Ala Ala Thr
        275                 280                 285

Val Cys Ile Cys Arg Ser Gly Phe Phe Arg Ala Asp Ala Asp Pro Ala
    290                 295                 300

Asp Ser Ala Cys Thr Ser Val Pro Ser Ala Pro Arg Ser Val Ile Ser
305                 310                 315                 320

Asn Val Asn Glu Thr Ser Leu Val Leu Glu Trp Ser Glu Pro Gln Asp
                325                 330                 335

Ala Gly Gly Arg Asp Asp Leu Leu Tyr Asn Val Ile Cys Lys Lys Cys
            340                 345                 350
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Ser Val Glu Arg Arg Leu Cys Ser Arg Cys Asp Asp Asn Val Glu Phe
        355                 360                 365

Val Pro Arg Gln Leu Gly Leu Thr Gly Leu Thr Glu Arg Arg Ile Tyr
    370                 375                 380

Ile Ser Lys Val Met Ala His Pro Gln Tyr Thr Phe Glu Ile Gln Ala
385                 390                 395                 400

Val Asn Gly Ile Ser Ser Lys Ser Pro Tyr Pro Pro His Phe Ala Ser
                405                 410                 415

Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Ala Val Pro Thr Met
            420                 425                 430

His Leu His Ser Ser Thr Gly Asn Ser Met Thr Leu Ser Trp Thr Pro
        435                 440                 445

Pro Glu Arg Pro Asn Gly Ile Ile Leu Asp Tyr Glu Ile Lys Tyr Ser
    450                 455                 460

Glu Lys Gln Gly Gln Gly Asp Gly Ile Ala Asn Thr Val Thr Ser Gln
465                 470                 475                 480

Lys Asn Ser Val Arg Leu Asp Gly Leu Lys Ala Asn Ala Arg Tyr Met
                485                 490                 495

Val Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly Arg Tyr Ser Leu
            500                 505                 510

Pro Thr Glu Phe Gln Thr Thr Ala Glu Asp Gly Ser Thr Ser Lys Thr
        515                 520                 525

Phe Gln Glu Leu Pro Leu Ile Val Gly Ser Ala Thr Ala Gly Leu Leu
    530                 535                 540

Phe Val Ile Val Val Val Ile Ile Ala Ile Val Cys Phe Arg Lys Gln
545                 550                 555                 560

Arg Asn Ser Thr Asp Pro Glu Tyr Thr Glu Lys Leu Gln Gln Tyr Val
                565                 570                 575

Thr Pro Gly Met Lys Val Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro
            580                 585                 590

Asn Glu Ala Val Arg Glu Phe Ala Lys Glu Ile Asp Ile Ser Cys Val
        595                 600                 605

Lys Ile Glu Glu Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys Arg
    610                 615                 620

Gly Arg Leu Lys Leu Pro Gly Arg Arg Glu Ile Phe Val Ala Ile Lys
625                 630                 635                 640

Thr Leu Lys Val Gly Tyr Thr Glu Arg Gln Arg Arg Asp Phe Leu Ser
                645                 650                 655

Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His Leu
            660                 665                 670

Glu Gly Val Val Thr Lys Ser Arg Pro Val Met Ile Ile Thr Glu Phe
        675                 680                 685

Met Glu Asn Cys Ala Leu Asp Ser Phe Leu Arg Leu Asn Asp Gly Gln
    690                 695                 700
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Phe Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly
705                 710                 715                 720

Met Lys Tyr Leu Ser Glu Met Asn Tyr Val His Arg Asp Leu Ala Ala
                725                 730                 735

Arg Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe
            740                 745                 750

Gly Leu Ser Arg Phe Leu Glu Asp Asp Pro Ala Asp Pro Thr Tyr Thr
        755                 760                 765

Ser Ser Leu Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala
    770                 775                 780

Ile Ala Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly
785                 790                 795                 800

Ile Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp
                805                 810                 815

Met Ser Asn Gln Asp Val Ile Asn Ala Val Glu Gln Asp Tyr Arg Leu
            820                 825                 830

Pro Pro Pro Met Asp Cys Pro Thr Ala Leu His Gln Leu Met Leu Asp
        835                 840                 845

Cys Trp Val Arg Asp Arg Asn Leu Arg Pro Lys Phe Ala Gln Ile Val
    850                 855                 860

Asn Thr Leu Asp Lys Leu Ile Arg Asn Ala Ala Ser Leu Lys Val Ile
865                 870                 875                 880

Ala Ser Val Gln Ser Gly Val Ser Gln Pro Leu Leu Asp Arg Thr Val
                885                 890                 895

Pro Asp Tyr Thr Thr Phe Thr Thr Val Gly Asp Trp Leu Asp Ala Ile
            900                 905                 910

Lys Met Gly Arg Tyr Lys Glu Asn Phe Val Asn Ala Gly Phe Ala Ser
        915                 920                 925

Phe Asp Leu Val Ala Gln Met Thr Ala Glu Asp Leu Leu Arg Ile Gly
    930                 935                 940

Val Thr Leu Ala Gly His Gln Lys Lys Ile Leu Ser Ser Ile Gln Asp
945                 950                 955                 960

Met Arg Leu Gln Met Asn Gln Thr Leu Pro Val Gln Val
                965                 970
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(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4097 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 10..3042

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

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CGGCTTCTG ATG CCC GGC CCG GAG CGC ACC ATG GGG CCG TTG TGG TTC          48
          Met Pro Gly Pro Glu Arg Thr Met Gly Pro Leu Trp Phe
            1               5                  10

TGC TGT TTG CCC CTC GCC CTC TTG CCT CTG CTC GCC GCC GTG GAA GAG        96
Cys Cys Leu Pro Leu Ala Leu Leu Pro Leu Leu Ala Ala Val Glu Glu
     15                  20                  25

ACG CTG ATG GAC TCC ACA ACG GCC ACA GCA GAG CTG GGC TGG ATG GTG       144
Thr Leu Met Asp Ser Thr Thr Ala Thr Ala Glu Leu Gly Trp Met Val
 30                  35                  40                  45

CAT CCT CCC TCA GGG TGG GAA GAG GTG AGT GGA TAC GAT GAG AAC ATG       192
His Pro Pro Ser Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Asn Met
                 50                  55                  60

AAC ACC ATC CGC ACC TAC CAG GTG TGC AAC GTC TTT GAA TCC AGC CAA       240
Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Ser Ser Gln
            65                  70                  75

AAC AAC TGG CTG CGG ACC AAG TAC ATC CGG AGG CGA GGA GCG CAC CGC       288
Asn Asn Trp Leu Arg Thr Lys Tyr Ile Arg Arg Arg Gly Ala His Arg
        80                  85                  90

ATC CAC GTG GAG ATG AAA TTC TCC GTT CGG GAC TGC AGC AGC ATC CCC       336
Ile His Val Glu Met Lys Phe Ser Val Arg Asp Cys Ser Ser Ile Pro
     95                 100                 105

AAC GTC CCG GGC TCC TGT AAG GAG ACT TTT AAC CTC TAT TAC TAC GAA       384
Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu
110                 115                 120                 125

TCA GAC TTT GAC TCT GCC ACC AAG ACT TTT CCT AAC TGG ATG GAA AAC       432
Ser Asp Phe Asp Ser Ala Thr Lys Thr Phe Pro Asn Trp Met Glu Asn
                130                 135                 140

CCT TGG ATG AAG GTA GAT ACA ATT GCT GCC GAC GAG AGC TTC TCG CAG       480
Pro Trp Met Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser Gln
            145                 150                 155

GTG GAC CTT GGT GGG CGG GTG ATG AAG ATT AAC ACC GAG GTG CGC AGT       528
Val Asp Leu Gly Gly Arg Val Met Lys Ile Asn Thr Glu Val Arg Ser
        160                 165                 170

TTT GGG CCT GTC TCC AAA AAC GGT TTC TAC CTG GCC TTC CAG GAC TAC       576
Phe Gly Pro Val Ser Lys Asn Gly Phe Tyr Leu Ala Phe Gln Asp Tyr
    175                 180                 185

GGG GGC TGC ATG TCC TTG ATT GCA GTC CGT GTC TTT TAC CGC AAG TGT       624
Gly Gly Cys Met Ser Leu Ile Ala Val Arg Val Phe Tyr Arg Lys Cys
190                 195                 200                 205

CCC CGT GTG ATC CAG AAC GGG GCG GTC TTC CAG GAA ACC CTC TCG GGA       672
Pro Arg Val Ile Gln Asn Gly Ala Val Phe Gln Glu Thr Leu Ser Gly
                210                 215                 220

GCG GAG AGC ACA TCT CTG GTG GCA GCC CGG GGG ACG TGC ATC AGC AAT       720
Ala Glu Ser Thr Ser Leu Val Ala Ala Arg Gly Thr Cys Ile Ser Asn
            225                 230                 235

GCG GAG GAG GTG GAT GTG CCC ATC AAG CTG TAC TGC AAT GGG GAT GGC       768
Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly Asp Gly
        240                 245                 250

GAG TGG CTG GTG CCC ATC GGC CGC TGC ATG TGC AGG CCG GGC TAT GAG       816
Glu Trp Leu Val Pro Ile Gly Arg Cys Met Cys Arg Pro Gly Tyr Glu
    255                 260                 265
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TCG GTG GAG AAT GGG ACC GTC TGC AGA GGC TGC CCA TCA GGG ACC TTC        864
Ser Val Glu Asn Gly Thr Val Cys Arg Gly Cys Pro Ser Gly Thr Phe
270                 275                 280                 285

AAG GCC AGC CAA GGA GAT GAA GGA TGT GTC CAT TGT CCA ATT AAC AGC        912
Lys Ala Ser Gln Gly Asp Glu Gly Cys Val His Cys Pro Ile Asn Ser
                290                 295                 300

CGG ACG ACT TCG GAA GGG GCC ACG AAC TGC GTG TGC CGA AAC GGA TAT        960
Arg Thr Thr Ser Glu Gly Ala Thr Asn Cys Val Cys Arg Asn Gly Tyr
            305                 310                 315

TAC CGG GCA GAT GCT GAC CCC GTC GAC ATG CCA TGC ACC ACC ATC CCA       1008
Tyr Arg Ala Asp Ala Asp Pro Val Asp Met Pro Cys Thr Thr Ile Pro
        320                 325                 330

TCT GCC CCC CAG GCC GTG ATC TCC AGC GTG AAT GAA ACC TCC CTG ATG       1056
Ser Ala Pro Gln Ala Val Ile Ser Ser Val Asn Glu Thr Ser Leu Met
    335                 340                 345

CTG GAG TGG ACC CCA CCA CGA GAC TCA GGG GGC CGG GAG GAT CTG GTA       1104
Leu Glu Trp Thr Pro Pro Arg Asp Ser Gly Gly Arg Glu Asp Leu Val
350                 355                 360                 365

TAC AAC ATC ATC TGC AAG AGC TGT GGG TCA GGC CGT GGG GCG TGC ACG       1152
Tyr Asn Ile Ile Cys Lys Ser Cys Gly Ser Gly Arg Gly Ala Cys Thr
                370                 375                 380

CGC TGT GGG GAC AAC GTG CAG TTT GCC CCA CGC CAG CTG GGC CTG ACG       1200
Arg Cys Gly Asp Asn Val Gln Phe Ala Pro Arg Gln Leu Gly Leu Thr
            385                 390                 395

GAG CCT CGC ATC TAC ATC AGC GAC CTG CTG GCC CAC ACG CAG TAC ACC       1248
Glu Pro Arg Ile Tyr Ile Ser Asp Leu Leu Ala His Thr Gln Tyr Thr
        400                 405                 410

TTT GAG ATC CAG GCT GTG AAT GGG GTC ACC GAC CAG AGC CCC TTC TCC       1296
Phe Glu Ile Gln Ala Val Asn Gly Val Thr Asp Gln Ser Pro Phe Ser
    415                 420                 425

CCA CAG TTT GCA TCA GTG AAT ATC ACC ACC AAC CAG GCT GCT CCT TCA       1344
Pro Gln Phe Ala Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser
430                 435                 440                 445

GCC GTG TCC ATA ATG CAC CAG GTC AGC CGC ACT GTG GAC AGC ATT ACC       1392
Ala Val Ser Ile Met His Gln Val Ser Arg Thr Val Asp Ser Ile Thr
                450                 455                 460

CTC TCG TGG TCT CAA CCT GAC CAG CCC AAT GGA GTC ATC CTG GAT TAT       1440
Leu Ser Trp Ser Gln Pro Asp Gln Pro Asn Gly Val Ile Leu Asp Tyr
            465                 470                 475

GAG CTG CAA TAC TAT GAG AAG AAC CTG AGT GAG TTA AAT TCA ACA GCA       1488
Glu Leu Gln Tyr Tyr Glu Lys Asn Leu Ser Glu Leu Asn Ser Thr Ala
        480                 485                 490

GTG AAG AGC CCC ACC AAC ACT GTG ACA GTG CAA AAC CTC AAA GCT GGC       1536
Val Lys Ser Pro Thr Asn Thr Val Thr Val Gln Asn Leu Lys Ala Gly
    495                 500                 505

ACC ATC TAT GTC TTC CAA GTG CGA GCA CGT ACC GTG GCT GGG TAT GGC       1584
Thr Ile Tyr Val Phe Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly
510                 515                 520                 525

CGG TAT AGT GGC AAG ATG TAC TTC CAG ACC ATG ACT GAA GCC GAG TAC       1632
Arg Tyr Ser Gly Lys Met Tyr Phe Gln Thr Met Thr Glu Ala Glu Tyr
                530                 535                 540
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CAG ACC AGT GTC CAG GAG AAG CTG CCA CTC ATC ATT GGC TCC TCT GCA      1680
Gln Thr Ser Val Gln Glu Lys Leu Pro Leu Ile Ile Gly Ser Ser Ala
            545                 550                 555

GCA GGA CTG GTG TTT CTC ATT GCT GTT GTC GTC ATC ATT ATT GTC TGC      1728
Ala Gly Leu Val Phe Leu Ile Ala Val Val Val Ile Ile Ile Val Cys
        560                 565                 570

AAC AGA AGA CGG GGC TTT GAA CGT GCT GAC TCT GAG TAC ACT GAC AAG      1776
Asn Arg Arg Arg Gly Phe Glu Arg Ala Asp Ser Glu Tyr Thr Asp Lys
    575                 580                 585

CTG CAG CAC TAT ACC AGT GGC CAC AGT ACG TAC CGT GGT CCC CCG CCA      1824
Leu Gln His Tyr Thr Ser Gly His Ser Thr Tyr Arg Gly Pro Pro Pro
590                 595                 600                 605

GGC CTG GGG GTC CGC TCT CTC TTC GTG ACT CCA GGG ATG AAG ATT TAT      1872
Gly Leu Gly Val Arg Ser Leu Phe Val Thr Pro Gly Met Lys Ile Tyr
                610                 615                 620

ATC GAT CCA TTT ACC TAC GAA GAT CCC AAT GAG GCT GTC AGG GAA TTT      1920
Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe
            625                 630                 635

GCA AAA GAA ATT GAT ATC TCC TGT GTG AAA ATC GAG CAG GTG ATT GGG      1968
Ala Lys Glu Ile Asp Ile Ser Cys Val Lys Ile Glu Gln Val Ile Gly
        640                 645                 650

GCA GGG GAG TTT GGT GAG GTG TGC AGT GGG CAT CTC AAG CTT CCT GGC      2016
Ala Gly Glu Phe Gly Glu Val Cys Ser Gly His Leu Lys Leu Pro Gly
    655                 660                 665

AAA AGA GAG ATC TTT GTG GCC ATC AAG ACC CTG AAG TCT GGT TAC ACA      2064
Lys Arg Glu Ile Phe Val Ala Ile Lys Thr Leu Lys Ser Gly Tyr Thr
670                 675                 680                 685

GAG AAG CAG AGA CGG GAC TTC CTG AGT GAA GCC AGC ATC ATG GGG CAG      2112
Glu Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln
                690                 695                 700

TTT GAC CAC CCC AAT GTC ATC CAC CTG GAA GGG GTG GTG ACC AAG AGT      2160
Phe Asp His Pro Asn Val Ile His Leu Glu Gly Val Val Thr Lys Ser
            705                 710                 715

TCC CCA GTC ATG ATC ATT ACA GAG TTC ATG GAG AAT GGC TCG TTG GAC      2208
Ser Pro Val Met Ile Ile Thr Glu Phe Met Glu Asn Gly Ser Leu Asp
        720                 725                 730

TCC TTC TTG AGG CAA AAT GAT GGG CAG TTC ACA GTG ATC CAG CTG GTG      2256
Ser Phe Leu Arg Gln Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val
    735                 740                 745

GGC ATG TTG CGT GGC ATT GCA GCA GGC ATG AAG TAC CTG GCT GAT ATG      2304
Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala Asp Met
750                 755                 760                 765

AAC TAC GTG CAC CGG GAC CTG GCT GCC CGC AAC ATC CTG GTC AAC AGC      2352
Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser
                770                 775                 780

AAC CTG GTC TGC AAG GTG TCC GAC TTC GGC CTC TCC CGT TTC CTG GAG      2400
Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu
            785                 790                 795

GAT GAC ACC TCT GAT CCC ACT TAC ACC AGC GCA CTG GGT GGA AAG ATC      2448
Asp Asp Thr Ser Asp Pro Thr Tyr Thr Ser Ala Leu Gly Gly Lys Ile
        800                 805                 810
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CCA ATA CGG TGG ACA GCG CCT GAG GCA ATT CAG TAC CGA AAA TTC ACA      2496
Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr
    815                 820                 825

TCA GCC AGC GAT GTG TGG AGC TAT GGA ATA GTC ATG TGG GAG GTG ATG      2544
Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met
830                 835                 840                 845

TCG TAC GGC GAG CGG CCT TAC TGG GAC ATG ACC AAT CAA GAT GTG ATA      2592
Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Thr Asn Gln Asp Val Ile
                850                 855                 860

AAT GCT ATT GAG CAG GAC TAT CGG CTA CCA CCC CCT ATG GAT TGT CCA      2640
Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro
            865                 870                 875

AAT GCC CTG CAC CAG CTA ATG CTT GAC TGC TGG CAG AAG GAT CGA AAC      2688
Asn Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn
        880                 885                 890

CAC AGA CCC AAA TTT GGA CAG ATT GTC AAC ACT TTA GAC AAA ATG ATC      2736
His Arg Pro Lys Phe Gly Gln Ile Val Asn Thr Leu Asp Lys Met Ile
    895                 900                 905

CGA AAT CCT AAT AGT CTG AAA GCC ATG GCA CCT CTC TCC TCT GGG GTT      2784
Arg Asn Pro Asn Ser Leu Lys Ala Met Ala Pro Leu Ser Ser Gly Val
910                 915                 920                 925

AAC CTC CCT CTA CTT GAC CGC ACA ATC CCA GAT TAT ACC AGC TTC AAC      2832
Asn Leu Pro Leu Leu Asp Arg Thr Ile Pro Asp Tyr Thr Ser Phe Asn
                930                 935                 940

ACT GTG GAT GAA TGG CTG GAT GCC ATC AAG ATG AGC CAG TAC AAG GAG      2880
Thr Val Asp Glu Trp Leu Asp Ala Ile Lys Met Ser Gln Tyr Lys Glu
            945                 950                 955

AGC TTT GCC AGT GCT GGC TTC ACC ACC TTT GAT ATA GTA TCT CAG ATG      2928
Ser Phe Ala Ser Ala Gly Phe Thr Thr Phe Asp Ile Val Ser Gln Met
        960                 965                 970

ACT GTA GAG GAC ATT CTA CGA GTT GGG GTC ACT TTA GCA GGA CAC CAG      2976
Thr Val Glu Asp Ile Leu Arg Val Gly Val Thr Leu Ala Gly His Gln
    975                 980                 985

AAG AAA ATT CTG AAC AGT ATC CAG GTG ATG AGA GCA CAG ATG AAC CAA      3024
Lys Lys Ile Leu Asn Ser Ile Gln Val Met Arg Ala Gln Met Asn Gln
990                 995                1000                1005

ATT CAG TCT GTG GAG GTT TGATAGCAAC ACGTCCTCGT GCTCCACTTC             3072
Ile Gln Ser Val Glu Val
            1010

CTTGAGGCCC TGCTCCCCTC TGCCCCTGTG TGTCTGAGCT CCAGTTCTTG AGTGTTCTGC    3132

GTGGATCAGA GACAGGCAGC TGCTCTGAGG ATCATGGCAA CAGGAAGAAA TGCCCTATCA    3192

TTGACAACGA GAAGTCATCA AGAGGTGAAA CAATGGAAAA CAATGGAAAA AGGGAACAAG    3252

TAAAGACAGC TATTTTGAAA ACCGAAAACA AACAGTGAAT TATTTTTAAA TAATAATAAA    3312

GCAATTGCAG TCTTGAAAAG GGCTCCAAGA CCAATGGGAG TCTCCAAAGG AAGAGAATAG    3372

AGCAGCTTCA TCTATTTCCT CTTACACAAG GGTTGCTGCA GCTGGGCCCA GACACTTCTG    3432

GAGTAACGAG ACTTTTCAAG AAGATGAATG CAAAGAATGG TCACAAGAAG CACTTCTCTT    3492

TCTCACATGG GATGGCAGCT CTGGGAATGC CCGGCAGTCC TTCCTGAAAG CCCTGTTGGC    3552
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AAATCGAAGA GGAGAGCCGA AGCTCTTTGG TGCTGTGGAA CCAAGTGCAT CTCAGAAATT 3612

GTTGGACTTC TACAAAAGCT GAAGACATTC TTTTTTTTTA AACAAGTAAA CTGATACTAG 3672

AAGAGGCTGT TTCCGTCAAA TGAGAAGGAA TCTGTAACAC TGGCCCGGGG GGGGTGGGGA 3732

ATGGGGGAAA TCAGTCCTTT TTACATCTCT TTATTTTCTC TTGTCATGGA ACAGTTTTGT 3792

GAGTGACAGT TTCCTAAGGG TCCGTCCATC CACCCTCCAA TGGCATCATT GTTTCATACA 3852

TATCATATGC ACAAGACTTA TAGTGATGTC CTCACTCGAT GCCAATGATC TTTCCCCAGA 3912

AGACTTCCCA AGTACAGTAT GTAGTAGATT TTGATTACAA ATGCTGACGT GTACCTTTAT 3972

TTTTCGGTTG TCGTTGTTGG GAGATTCGTC CTTTTACCTT GCTTTGTTAA CACCAATTTG 4032

TGAGTTTGGG GTTGGAATTT TTTTGGTCGA TTGGGGTTGT TTTTTTTTTT TTTTTTTTTT 4092

AACCG 4097

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1011 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

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Met Pro Gly Pro Glu Arg Thr Met Gly Pro Leu Trp Phe Cys Cys Leu
 1               5                  10                  15

Pro Leu Ala Leu Leu Pro Leu Leu Ala Ala Val Glu Glu Thr Leu Met
            20                  25                  30

Asp Ser Thr Thr Ala Thr Ala Glu Leu Gly Trp Met Val His Pro Pro
        35                  40                  45

Ser Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Asn Met Asn Thr Ile
    50                  55                  60

Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Ser Ser Gln Asn Asn Trp
65                  70                  75                  80

Leu Arg Thr Lys Tyr Ile Arg Arg Arg Gly Ala His Arg Ile His Val
                85                  90                  95

Glu Met Lys Phe Ser Val Arg Asp Cys Ser Ser Ile Pro Asn Val Pro
            100                 105                 110

Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu Ser Asp Phe
        115                 120                 125

Asp Ser Ala Thr Lys Thr Phe Pro Asn Trp Met Glu Asn Pro Trp Met
    130                 135                 140

Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser Gln Val Asp Leu
145                 150                 155                 160

Gly Gly Arg Val Met Lys Ile Asn Thr Glu Val Arg Ser Phe Gly Pro
                165                 170                 175

Val Ser Lys Asn Gly Phe Tyr Leu Ala Phe Gln Asp Tyr Gly Gly Cys
            180                 185                 190
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Met Ser Leu Ile Ala Val Arg Val Phe Tyr Arg Lys Cys Pro Arg Val
        195                 200                 205

Ile Gln Asn Gly Ala Val Phe Gln Glu Thr Leu Ser Gly Ala Glu Ser
    210                 215                 220

Thr Ser Leu Val Ala Ala Arg Gly Thr Cys Ile Ser Asn Ala Glu Glu
225                 230                 235                 240

Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly Asp Gly Glu Trp Leu
                245                 250                 255

Val Pro Ile Gly Arg Cys Met Cys Arg Pro Gly Tyr Glu Ser Val Glu
            260                 265                 270

Asn Gly Thr Val Cys Arg Gly Cys Pro Ser Gly Thr Phe Lys Ala Ser
        275                 280                 285

Gln Gly Asp Glu Gly Cys Val His Cys Pro Ile Asn Ser Arg Thr Thr
    290                 295                 300

Ser Glu Gly Ala Thr Asn Cys Val Cys Arg Asn Gly Tyr Tyr Arg Ala
305                 310                 315                 320

Asp Ala Asp Pro Val Asp Met Pro Cys Thr Thr Ile Pro Ser Ala Pro
                325                 330                 335

Gln Ala Val Ile Ser Ser Val Asn Glu Thr Ser Leu Met Leu Glu Trp
            340                 345                 350

Thr Pro Pro Arg Asp Ser Gly Gly Arg Glu Asp Leu Val Tyr Asn Ile
        355                 360                 365

Ile Cys Lys Ser Cys Gly Ser Gly Arg Gly Ala Cys Thr Arg Cys Gly
    370                 375                 380

Asp Asn Val Gln Phe Ala Pro Arg Gln Leu Gly Leu Thr Glu Pro Arg
385                 390                 395                 400

Ile Tyr Ile Ser Asp Leu Leu Ala His Thr Gln Tyr Thr Phe Glu Ile
                405                 410                 415

Gln Ala Val Asn Gly Val Thr Asp Gln Ser Pro Phe Ser Pro Gln Phe
            420                 425                 430

Ala Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Ala Val Ser
        435                 440                 445

Ile Met His Gln Val Ser Arg Thr Val Asp Ser Ile Thr Leu Ser Trp
    450                 455                 460

Ser Gln Pro Asp Gln Pro Asn Gly Val Ile Leu Asp Tyr Glu Leu Gln
465                 470                 475                 480

Tyr Tyr Glu Lys Asn Leu Ser Glu Leu Asn Ser Thr Ala Val Lys Ser
                485                 490                 495

Pro Thr Asn Thr Val Thr Val Gln Asn Leu Lys Ala Gly Thr Ile Tyr
            500                 505                 510

Val Phe Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly Arg Tyr Ser
        515                 520                 525

Gly Lys Met Tyr Phe Gln Thr Met Thr Glu Ala Glu Tyr Gln Thr Ser
    530                 535                 540
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Val Gln Glu Lys Leu Pro Leu Ile Ile Gly Ser Ser Ala Ala Gly Leu
545                 550                 555                 560

Val Phe Leu Ile Ala Val Val Val Ile Ile Ile Val Cys Asn Arg Arg
                565                 570                 575

Arg Gly Phe Glu Arg Ala Asp Ser Glu Tyr Thr Asp Lys Leu Gln His
            580                 585                 590

Tyr Thr Ser Gly His Ser Thr Tyr Arg Gly Pro Pro Pro Gly Leu Gly
        595                 600                 605

Val Arg Ser Leu Phe Val Thr Pro Gly Met Lys Ile Tyr Ile Asp Pro
    610                 615                 620

Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe Ala Lys Glu
625                 630                 635                 640

Ile Asp Ile Ser Cys Val Lys Ile Glu Gln Val Ile Gly Ala Gly Glu
                645                 650                 655

Phe Gly Glu Val Cys Ser Gly His Leu Lys Leu Pro Gly Lys Arg Glu
            660                 665                 670

Ile Phe Val Ala Ile Lys Thr Leu Lys Ser Gly Tyr Thr Glu Lys Gln
        675                 680                 685

Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Asp His
    690                 695                 700

Pro Asn Val Ile His Leu Glu Gly Val Val Thr Lys Ser Ser Pro Val
705                 710                 715                 720

Met Ile Ile Thr Glu Phe Met Glu Asn Gly Ser Leu Asp Ser Phe Leu
                725                 730                 735

Arg Gln Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly Met Leu
            740                 745                 750

Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala Asp Met Asn Tyr Val
        755                 760                 765

His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val
    770                 775                 780

Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu Asp Asp Thr
785                 790                 795                 800

Ser Asp Pro Thr Tyr Thr Ser Ala Leu Gly Gly Lys Ile Pro Ile Arg
                805                 810                 815

Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr Ser Ala Ser
            820                 825                 830

Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly
        835                 840                 845

Glu Arg Pro Tyr Trp Asp Met Thr Asn Gln Asp Val Ile Asn Ala Ile
    850                 855                 860

Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro Asn Ala Leu
865                 870                 875                 880

His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn His Arg Pro
                885                 890                 895
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Lys Phe Gly Gln Ile Val Asn Thr Leu Asp Lys Met Ile Arg Asn Pro
            900                 905                 910

Asn Ser Leu Lys Ala Met Ala Pro Leu Ser Ser Gly Val Asn Leu Pro
        915                 920                 925

Leu Leu Asp Arg Thr Ile Pro Asp Tyr Thr Ser Phe Asn Thr Val Asp
    930                 935                 940

Glu Trp Leu Asp Ala Ile Lys Met Ser Gln Tyr Lys Glu Ser Phe Ala
945                 950                 955                 960

Ser Ala Gly Phe Thr Thr Phe Asp Ile Val Ser Gln Met Thr Val Glu
                965                 970                 975

Asp Ile Leu Arg Val Gly Val Thr Leu Ala Gly His Gln Lys Lys Ile
            980                 985                 990

Leu Asn Ser Ile Gln Val Met Arg Ala Gln Met Asn Gln Ile Gln Ser
        995                 1000                1005

Val Glu Val
    1010
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(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3591 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..2965

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

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C GGG GTC TCC TCG AGG GCG CGG CGG CCG CCG GGC AGC AGC AGG AGC          46
  Gly Val Ser Ser Arg Ala Arg Arg Pro Pro Gly Ser Ser Arg Ser
    1               5                  10                  15

AGC AGG AGG GGG GTG ACC TCG GAG CTG GCA TGG ACA ACC CAT CCG GAG        94
Ser Arg Arg Gly Val Thr Ser Glu Leu Ala Trp Thr Thr His Pro Glu
                20                  25                  30

ACG GGG TGG GAA GAG GTC AGT GGT TAC GAC GAG GCT ATG AAC CCC ATC       142
Thr Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Ala Met Asn Pro Ile
            35                  40                  45

CGC ACA TAC CAG GTG TGC AAC GTG CGG GAG GCC AAC CAG AAC AAC TGG       190
Arg Thr Tyr Gln Val Cys Asn Val Arg Glu Ala Asn Gln Asn Asn Trp
        50                  55                  60

CTT CGC ACC AAG TTC ATT CAG CGC CAG GAC GTC CAG CGT GTC TAC GTG       238
Leu Arg Thr Lys Phe Ile Gln Arg Gln Asp Val Gln Arg Val Tyr Val
    65                  70                  75

GAG CTG AAA TTC ACT GTG CGG GAC TGC AAC AGC ATC CCC AAC ATC CCT       286
Glu Leu Lys Phe Thr Val Arg Asp Cys Asn Ser Ile Pro Asn Ile Pro
80                  85                  90                  95

GGT TCC TGC AAA GAG ACC TTC AAC CTC TTC TAT TAT GAG TCA GAT ACG       334
Gly Ser Cys Lys Glu Thr Phe Asn Leu Phe Tyr Tyr Glu Ser Asp Thr
                100                 105                 110
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GAT TCT GCC TCT GCC AAT AGC CCT TTC TGG ATG GAG AAC CCC TAT ATC        382
Asp Ser Ala Ser Ala Asn Ser Pro Phe Trp Met Glu Asn Pro Tyr Ile
            115                 120                 125

AAA GTG GAT ACA ATT GCT CCG GAT GAG AGC TTC TCC AAA CTG GAG TCC        430
Lys Val Asp Thr Ile Ala Pro Asp Glu Ser Phe Ser Lys Leu Glu Ser
        130                 135                 140

GGC CGT GTG AAC ACC AAG GTG CGC AGC TTT GGG CCG CTC TCC AAG AAT        478
Gly Arg Val Asn Thr Lys Val Arg Ser Phe Gly Pro Leu Ser Lys Asn
    145                 150                 155

GGC TTT TAT CTG GCT TTC CAG GAC CTG GGG GCC TGC ATG TCC CTT ATC        526
Gly Phe Tyr Leu Ala Phe Gln Asp Leu Gly Ala Cys Met Ser Leu Ile
160                 165                 170                 175

TCC GTC CGG GCT TTC TAC AAG AAA TGT TCC AAC ACC ATC GCT GGC TTT        574
Ser Val Arg Ala Phe Tyr Lys Lys Cys Ser Asn Thr Ile Ala Gly Phe
                180                 185                 190

GCT ATC TTC CCG GAG ACC CTA ACG GGG GCT GAG CCC ACG TCG CTG GTC        622
Ala Ile Phe Pro Glu Thr Leu Thr Gly Ala Glu Pro Thr Ser Leu Val
            195                 200                 205

ATT GCG CCG GGC ACC TGC ATC CCC AAC GCA GTG GAA GTG TCT GTG CCC        670
Ile Ala Pro Gly Thr Cys Ile Pro Asn Ala Val Glu Val Ser Val Pro
        210                 215                 220

CTG AAG CTG TAC TGC AAC GGT GAT GGC GAG TGG ATG GTG CCT GTG GGA        718
Leu Lys Leu Tyr Cys Asn Gly Asp Gly Glu Trp Met Val Pro Val Gly
    225                 230                 235

GCG TGC ACG TGT GCT GCT GGG TAC GAG CCA GCC ATG AAG GAT ACC CAG        766
Ala Cys Thr Cys Ala Ala Gly Tyr Glu Pro Ala Met Lys Asp Thr Gln
240                 245                 250                 255

TGC CAA GCA TGC GGC CCG GGG ACG TTC AAA TCC AAG CAG GGC GAG GGC        814
Cys Gln Ala Cys Gly Pro Gly Thr Phe Lys Ser Lys Gln Gly Glu Gly
                260                 265                 270

CCC TGC TCC CCC TGC CCT CCC AAC AGC CGC ACC ACC GCG GGG GCA GCC        862
Pro Cys Ser Pro Cys Pro Pro Asn Ser Arg Thr Thr Ala Gly Ala Ala
            275                 280                 285

ACA GTC TGC ATA TGT CGC AGC GGC TTC TTC CGA GCA GAC GCG GAC CCC        910
Thr Val Cys Ile Cys Arg Ser Gly Phe Phe Arg Ala Asp Ala Asp Pro
        290                 295                 300

GCA GAC AGC GCC TGC ACC AGT GTG CCC TCA GCC CCA CGC AGC GTC ATC        958
Ala Asp Ser Ala Cys Thr Ser Val Pro Ser Ala Pro Arg Ser Val Ile
    305                 310                 315

TCC AAC GTG AAT GAG ACG TCG TTG GTG CTG GAG TGG AGC GAG CCG CAG       1006
Ser Asn Val Asn Glu Thr Ser Leu Val Leu Glu Trp Ser Glu Pro Gln
320                 325                 330                 335

GAC GCG GGC GGG CGG GAT GAC CTG CTC TAC AAC GTC ATC TGC AAG AAG       1054
Asp Ala Gly Gly Arg Asp Asp Leu Leu Tyr Asn Val Ile Cys Lys Lys
                340                 345                 350

TGC AGC GTG GAG CGG CGG CTG TGC AGC CGC TGC GAC GAC AAC GTG GAG       1102
Cys Ser Val Glu Arg Arg Leu Cys Ser Arg Cys Asp Asp Asn Val Glu
            355                 360                 365

TTC GTG CCG CGC CAG CTG GGC CTC ACT GGC CTC ACT GAG CGA CGC ATC       1150
Phe Val Pro Arg Gln Leu Gly Leu Thr Gly Leu Thr Glu Arg Arg Ile
        370                 375                 380
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TAC ATC AGC AAG GTG ATG GCC CAC CCC CAG TAC ACC TTC GAG ATC CAG      1198
Tyr Ile Ser Lys Val Met Ala His Pro Gln Tyr Thr Phe Glu Ile Gln
    385                 390                 395

GCG GTG AAT GGC ATC TCC AGC AAG AGC CCC TAC CCT CCC CAT TTT GCC      1246
Ala Val Asn Gly Ile Ser Ser Lys Ser Pro Tyr Pro Pro His Phe Ala
400                 405                 410                 415

TCC GTC AAC ATC ACG ACC AAC CAG GCA GCC CCA TCT GCC GTG CCC ACC      1294
Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Ala Val Pro Thr
                420                 425                 430

ATG CAT CTG CAC AGC AGC ACC GGG AAC AGC ATG ACA CTG TCA TGG ACT      1342
Met His Leu His Ser Ser Thr Gly Asn Ser Met Thr Leu Ser Trp Thr
            435                 440                 445

CCC CCG GAA AGG CCC AAC GGC ATC ATT CTC GAC TAT GAA ATC AAG TAC      1390
Pro Pro Glu Arg Pro Asn Gly Ile Ile Leu Asp Tyr Glu Ile Lys Tyr
        450                 455                 460

TCC GAG AAG CAA GGC CAG GGT GAC GGC ATT GCC AAC ACT GTC ACC AGC      1438
Ser Glu Lys Gln Gly Gln Gly Asp Gly Ile Ala Asn Thr Val Thr Ser
    465                 470                 475

CAG AAG AAC TCG GTG CGG CTG GAC GGA CTG AAG GCC AAT GCT CGG TAC      1486
Gln Lys Asn Ser Val Arg Leu Asp Gly Leu Lys Ala Asn Ala Arg Tyr
480                 485                 490                 495

ATG GTG CAG GTC CGG GCG CGC ACA GTG GCT GGA TAC GGC CGC TAC AGC      1534
Met Val Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly Arg Tyr Ser
                500                 505                 510

CTC CCC ACC GAG TTC CAG ACG ACT GCG GAG GAT GGC TCC ACC AGC AAG      1582
Leu Pro Thr Glu Phe Gln Thr Thr Ala Glu Asp Gly Ser Thr Ser Lys
            515                 520                 525

ACT TTC CAG GAG CTT CCT CTC ATC GTG GGT TCA GCC ACC GCG GGA CTG      1630
Thr Phe Gln Glu Leu Pro Leu Ile Val Gly Ser Ala Thr Ala Gly Leu
        530                 535                 540

CTG TTT GTC ATC GTG GTG GTC ATC ATC GCT ATT GTC TGC TTC AGG AAA      1678
Leu Phe Val Ile Val Val Val Ile Ile Ala Ile Val Cys Phe Arg Lys
    545                 550                 555

GGG ATG GTT ACT GAA CAA CTC CTC TCG TCT CCT TTG GGC AGG AAG CAG      1726
Gly Met Val Thr Glu Gln Leu Leu Ser Ser Pro Leu Gly Arg Lys Gln
560                 565                 570                 575

CGC AAC AGC ACA GAT CCC GAG TAC ACA GAG AAG CTG CAG CAA TAT GTC      1774
Arg Asn Ser Thr Asp Pro Glu Tyr Thr Glu Lys Leu Gln Gln Tyr Val
                580                 585                 590

ACT CCT GGG ATG AAG GTC TAC ATT GAC CCC TTC ACC TAT GAA GAC CCA      1822
Thr Pro Gly Met Lys Val Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro
            595                 600                 605

AAT GAA GCT GTC CGG GAA TTC GCC AAA GAG ATT GAT ATC TCC TGT GTC      1870
Asn Glu Ala Val Arg Glu Phe Ala Lys Glu Ile Asp Ile Ser Cys Val
        610                 615                 620

AAA ATT GAG GAG GTC ATT GGA GCA GGA GAG TTT GGT GAG GTG TGC CGT      1918
Lys Ile Glu Glu Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys Arg
    625                 630                 635

GGG CGC CTG AAG CTG CCT GGC CGC CGT GAG ATC TTT GTG GCC ATC AAG      1966
Gly Arg Leu Lys Leu Pro Gly Arg Arg Glu Ile Phe Val Ala Ile Lys
640                 645                 650                 655
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ACA CTG AAG GTG GGC TAC ACA GAG AGG CAG CGG CGG GAC TTC CTG AGT      2014
Thr Leu Lys Val Gly Tyr Thr Glu Arg Gln Arg Arg Asp Phe Leu Ser
                660                 665                 670

GAG GCC AGC ATC ATG GGC CAG TTC GAC CAC CCC AAC ATC ATC CAC CTG      2062
Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His Leu
            675                 680                 685

GAG GGC GTG GTG ACC AAG AGC CGC CCT GTC ATG ATC ATC ACA GAG TTC      2110
Glu Gly Val Val Thr Lys Ser Arg Pro Val Met Ile Ile Thr Glu Phe
        690                 695                 700

ATG GAG AAC TGC GCT CTC GAC TCC TTC CTC CGG CTG AAT GAT GGG CAG      2158
Met Glu Asn Cys Ala Leu Asp Ser Phe Leu Arg Leu Asn Asp Gly Gln
    705                 710                 715

TTC ACG GTC ATC CAG CTG GTG GGG ATG CTG CGA GGC ATC GCT GCT GGC      2206
Phe Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly
720                 725                 730                 735

ATG AAG TAC CTC TCA GAG ATG AAC TAC GTG CAC CGA GAC CTG GCT GCC      2254
Met Lys Tyr Leu Ser Glu Met Asn Tyr Val His Arg Asp Leu Ala Ala
                740                 745                 750

CGC AAC ATC CTG GTC AAC AGC AAC TTG GTC TGC AAA GTG TCT GAC TTC      2302
Arg Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe
            755                 760                 765

GGG CTC TCC CGC TTT TTG GAG GAT GAT CCA GCC GAC CCC ACC TAC ACC      2350
Gly Leu Ser Arg Phe Leu Glu Asp Asp Pro Ala Asp Pro Thr Tyr Thr
        770                 775                 780

AGC TCC CTG GGA GGC AAG ATC CCC ATC AGG TGG ACA GCT CCT GAG GCC      2398
Ser Ser Leu Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala
    785                 790                 795

ATC GCC TAC CGC AAA TTC ACG TCG GCC AGC GAC GTG TGG AGC TAC GGC      2446
Ile Ala Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly
800                 805                 810                 815

ATC GTC ATG TGG GAA GTG ATG TCC TAC GGG GAG CGA CCC TAC TGG GAC      2494
Ile Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp
                820                 825                 830

ATG TCC AAC CAG GAT GTG ATC AAC GCG GTG GAG CAG GAT TAC CGC CTG      2542
Met Ser Asn Gln Asp Val Ile Asn Ala Val Glu Gln Asp Tyr Arg Leu
            835                 840                 845

CCA CCC CCC ATG GAC TGC CCC ACA GCA CTG CAC CAG CTG ATG CTG GAC      2590
Pro Pro Pro Met Asp Cys Pro Thr Ala Leu His Gln Leu Met Leu Asp
        850                 855                 860

TGC TGG GTG CGG GAC CGC AAC CTG CGG CCC AAG TTT GCA CAG ATT GTC      2638
Cys Trp Val Arg Asp Arg Asn Leu Arg Pro Lys Phe Ala Gln Ile Val
    865                 870                 875

AAC ACG CTG GAC AAG CTG ATC CGC AAT GCT GCC AGC CTG AAG GTC ATC      2686
Asn Thr Leu Asp Lys Leu Ile Arg Asn Ala Ala Ser Leu Lys Val Ile
880                 885                 890                 895

GCC AGC GTC CAG TCC GGT GTC TCC CAG CCG CTC CTG GAC CGC ACC GTG      2734
Ala Ser Val Gln Ser Gly Val Ser Gln Pro Leu Leu Asp Arg Thr Val
                900                 905                 910

CCC GAT TAC ACC ACC TTC ACC ACC GTG GGA GAC TGG CTG GAT GCC ATC      2782
Pro Asp Tyr Thr Thr Phe Thr Thr Val Gly Asp Trp Leu Asp Ala Ile
            915                 920                 925
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AAA ATG GGA CGG TAC AAG GAG AAC TTC GTC AAC GCC GGC TTC GCC TCC      2830
Lys Met Gly Arg Tyr Lys Glu Asn Phe Val Asn Ala Gly Phe Ala Ser
        930                 935                 940

TTT GAC CTG GTG GCA CAG ATG ACA GCA GAG GAC CTG CTA AGG ATA GGA      2878
Phe Asp Leu Val Ala Gln Met Thr Ala Glu Asp Leu Leu Arg Ile Gly
    945                 950                 955

GTG ACG CTA GCA GGG CAC CAG AAG AAG ATC CTG AGC AGC ATT CAG GAC      2926
Val Thr Leu Ala Gly His Gln Lys Lys Ile Leu Ser Ser Ile Gln Asp
960                 965                 970                 975

ATG AGG CTG CAG ATG AAC CAG ACG CTG CCG GTT CAG GTT TGACCGCAGG       2975
Met Arg Leu Gln Met Asn Gln Thr Leu Pro Val Gln Val
                980                 985

GACTCTGCAT TGGAACGGAC TGAGGGAACC TGCCAACCAG GTTCTGTTTG CGGTGCAGCC    3035

CGGCTTCCCG ATTTCCCCTT CCCGTGGCGC TCCTCTGCCT CGGACGCTCG CCGGGGACAG    3095

GCTGGGCCGG GCCACCCTTC CCTGGATCAG AGGCACTCGT GCCGGGAGGG AGCCCGGCTT    3155

TTCGTCCCGT GTCCCGCAGC GGCGAGGCAG TGAACGCAGT CTTCATATTG AAGATGGATT    3215

ATGGGACGGA GATGGCGCAT CCGCTTCCCG CCCTGTCTCA GTGCTCATCA GTTTGAAGAG    3275

ATGTTCTGCT TCTTGGATTT CTTTACACCC CGGTTTTCCC CCCTCGAGTC CTCACTTCCC    3335

CCTATCCCTG AGGCCACAGA CTGTTGACCC GTCCGCTGAG TCCGTCAGAC GCTCCGAAGC    3395

CTTCCCCGAG CCCGGTCCCC GCGTGGAGAC GGCGCCAGGG ACGGGGCTAC GGCCCCAGAC    3455

AATCACTCCA CCCCTCCGCA CGAGGGTCCT CACTGGGACG TGTCTGAAGG GGAAAGGCTC    3515

TGCTCCCTTT TTGGCTTTGC ACGCCAGAAC CCGAACCCCG TGAGATTTAC TATGCAGGGA    3575

GTTAGGCAAA AAAAAG                                                    3591
```

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 988 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

```
Gly Val Ser Ser Arg Ala Arg Arg Pro Pro Gly Ser Ser Arg Ser Ser
  1               5                  10                  15

Arg Arg Gly Val Thr Ser Glu Leu Ala Trp Thr Thr His Pro Glu Thr
            20                  25                  30

Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Ala Met Asn Pro Ile Arg
        35                  40                  45

Thr Tyr Gln Val Cys Asn Val Arg Glu Ala Asn Gln Asn Asn Trp Leu
    50                  55                  60

Arg Thr Lys Phe Ile Gln Arg Gln Asp Val Gln Arg Val Tyr Val Glu
65                  70                  75                  80

Leu Lys Phe Thr Val Arg Asp Cys Asn Ser Ile Pro Asn Ile Pro Gly
                85                  90                  95
```

```
Ser Cys Lys Glu Thr Phe Asn Leu Phe Tyr Tyr Glu Ser Asp Thr Asp
            100                 105                 110

Ser Ala Ser Ala Asn Ser Pro Phe Trp Met Glu Asn Pro Tyr Ile Lys
        115                 120                 125

Val Asp Thr Ile Ala Pro Asp Glu Ser Phe Ser Lys Leu Glu Ser Gly
    130                 135                 140

Arg Val Asn Thr Lys Val Arg Ser Phe Gly Pro Leu Ser Lys Asn Gly
145                 150                 155                 160

Phe Tyr Leu Ala Phe Gln Asp Leu Gly Ala Cys Met Ser Leu Ile Ser
                165                 170                 175

Val Arg Ala Phe Tyr Lys Lys Cys Ser Asn Thr Ile Ala Gly Phe Ala
            180                 185                 190

Ile Phe Pro Glu Thr Leu Thr Gly Ala Glu Pro Thr Ser Leu Val Ile
        195                 200                 205

Ala Pro Gly Thr Cys Ile Pro Asn Ala Val Glu Val Ser Val Pro Leu
    210                 215                 220

Lys Leu Tyr Cys Asn Gly Asp Gly Glu Trp Met Val Pro Val Gly Ala
225                 230                 235                 240

Cys Thr Cys Ala Ala Gly Tyr Glu Pro Ala Met Lys Asp Thr Gln Cys
                245                 250                 255

Gln Ala Cys Gly Pro Gly Thr Phe Lys Ser Lys Gln Gly Glu Gly Pro
            260                 265                 270

Cys Ser Pro Cys Pro Pro Asn Ser Arg Thr Thr Ala Gly Ala Ala Thr
        275                 280                 285

Val Cys Ile Cys Arg Ser Gly Phe Phe Arg Ala Asp Ala Asp Pro Ala
    290                 295                 300

Asp Ser Ala Cys Thr Ser Val Pro Ser Ala Pro Arg Ser Val Ile Ser
305                 310                 315                 320

Asn Val Asn Glu Thr Ser Leu Val Leu Glu Trp Ser Glu Pro Gln Asp
                325                 330                 335

Ala Gly Gly Arg Asp Asp Leu Leu Tyr Asn Val Ile Cys Lys Lys Cys
            340                 345                 350

Ser Val Glu Arg Arg Leu Cys Ser Arg Cys Asp Asp Asn Val Glu Phe
        355                 360                 365

Val Pro Arg Gln Leu Gly Leu Thr Gly Leu Thr Glu Arg Arg Ile Tyr
    370                 375                 380

Ile Ser Lys Val Met Ala His Pro Gln Tyr Thr Phe Glu Ile Gln Ala
385                 390                 395                 400

Val Asn Gly Ile Ser Ser Lys Ser Pro Tyr Pro Pro His Phe Ala Ser
                405                 410                 415

Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Ala Val Pro Thr Met
            420                 425                 430

His Leu His Ser Ser Thr Gly Asn Ser Met Thr Leu Ser Trp Thr Pro
        435                 440                 445
```

```
Pro Glu Arg Pro Asn Gly Ile Ile Leu Asp Tyr Glu Ile Lys Tyr Ser
    450                 455                 460

Glu Lys Gln Gly Gln Gly Asp Gly Ile Ala Asn Thr Val Thr Ser Gln
465                 470                 475                 480

Lys Asn Ser Val Arg Leu Asp Gly Leu Lys Ala Asn Ala Arg Tyr Met
                485                 490                 495

Val Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly Arg Tyr Ser Leu
            500                 505                 510

Pro Thr Glu Phe Gln Thr Thr Ala Glu Asp Gly Ser Thr Ser Lys Thr
        515                 520                 525

Phe Gln Glu Leu Pro Leu Ile Val Gly Ser Ala Thr Ala Gly Leu Leu
    530                 535                 540

Phe Val Ile Val Val Val Ile Ile Ala Ile Val Cys Phe Arg Lys Gly
545                 550                 555                 560

Met Val Thr Glu Gln Leu Leu Ser Ser Pro Leu Gly Arg Lys Gln Arg
                565                 570                 575

Asn Ser Thr Asp Pro Glu Tyr Thr Glu Lys Leu Gln Gln Tyr Val Thr
            580                 585                 590

Pro Gly Met Lys Val Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn
        595                 600                 605

Glu Ala Val Arg Glu Phe Ala Lys Glu Ile Asp Ile Ser Cys Val Lys
    610                 615                 620

Ile Glu Glu Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys Arg Gly
625                 630                 635                 640

Arg Leu Lys Leu Pro Gly Arg Arg Glu Ile Phe Val Ala Ile Lys Thr
                645                 650                 655

Leu Lys Val Gly Tyr Thr Glu Arg Gln Arg Arg Asp Phe Leu Ser Glu
            660                 665                 670

Ala Ser Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His Leu Glu
        675                 680                 685

Gly Val Val Thr Lys Ser Arg Pro Val Met Ile Ile Thr Glu Phe Met
    690                 695                 700

Glu Asn Cys Ala Leu Asp Ser Phe Leu Arg Leu Asn Asp Gly Gln Phe
705                 710                 715                 720

Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met
                725                 730                 735

Lys Tyr Leu Ser Glu Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg
            740                 745                 750

Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly
        755                 760                 765

Leu Ser Arg Phe Leu Glu Asp Asp Pro Ala Asp Pro Thr Tyr Thr Ser
    770                 775                 780

Ser Leu Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile
785                 790                 795                 800
```

```
Ala Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile
                805                 810                 815

Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met
            820                 825                 830

Ser Asn Gln Asp Val Ile Asn Ala Val Glu Gln Asp Tyr Arg Leu Pro
        835                 840                 845

Pro Pro Met Asp Cys Pro Thr Ala Leu His Gln Leu Met Leu Asp Cys
    850                 855                 860

Trp Val Arg Asp Arg Asn Leu Arg Pro Lys Phe Ala Gln Ile Val Asn
865                 870                 875                 880

Thr Leu Asp Lys Leu Ile Arg Asn Ala Ala Ser Leu Lys Val Ile Ala
                885                 890                 895

Ser Val Gln Ser Gly Val Ser Gln Pro Leu Leu Asp Arg Thr Val Pro
            900                 905                 910

Asp Tyr Thr Thr Phe Thr Thr Val Gly Asp Trp Leu Asp Ala Ile Lys
        915                 920                 925

Met Gly Arg Tyr Lys Glu Asn Phe Val Asn Ala Gly Phe Ala Ser Phe
    930                 935                 940

Asp Leu Val Ala Gln Met Thr Ala Glu Asp Leu Leu Arg Ile Gly Val
945                 950                 955                 960

Thr Leu Ala Gly His Gln Lys Lys Ile Leu Ser Ser Ile Gln Asp Met
                965                 970                 975

Arg Leu Gln Met Asn Gln Thr Leu Pro Val Gln Val
            980                 985
```

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3254 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 32..2980

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

```
CGCTCTGCTC GCGCGCTGCT GCCCCGCCGA C ATG GAC CGC CGC CGC CTG CCG          52
                                   Met Asp Arg Arg Arg Leu Pro
                                     1               5

CTG CTG CTG CTC TGC GCT GCC CTC GGC TCC GCC GGG CGT CTG AGC GCC         100
Leu Leu Leu Leu Cys Ala Ala Leu Gly Ser Ala Gly Arg Leu Ser Ala
        10                  15                  20

CGC CCC GGC AAC GAA GTT AAT CTG CTG GAT TCA AAA ACA ATT CAA GGG         148
Arg Pro Gly Asn Glu Val Asn Leu Leu Asp Ser Lys Thr Ile Gln Gly
    25                  30                  35

GAG CTG GGC TGG ATC TCC TAC CCA TCA CAT GGG TGG GAA GAG ATT AGT         196
Glu Leu Gly Trp Ile Ser Tyr Pro Ser His Gly Trp Glu Glu Ile Ser
40                  45                  50                  55
```

```
GGT GTT GAT GAG CAT TAT ACT CCA ATC AGA ACT TAC CAA GAG AGC AAT        244
Gly Val Asp Glu His Tyr Thr Pro Ile Arg Thr Tyr Gln Glu Ser Asn
                60                  65                  70

GTT ATG GAT CAC AGT CAA AAC AAT TGG CTG CGA ACA AAC TGG ATT CCA        292
Val Met Asp His Ser Gln Asn Asn Trp Leu Arg Thr Asn Trp Ile Pro
            75                  80                  85

CGC AAT TCA GCG CAG AAG ATA TAT GTG GAG CTC AAG TTT ACC TTG AGG        340
Arg Asn Ser Ala Gln Lys Ile Tyr Val Glu Leu Lys Phe Thr Leu Arg
        90                  95                  100

GAC TGC AAT AGT ATC CCT CTA GTT CTG GGC ACT TGC AAA GAG ACT TTC        388
Asp Cys Asn Ser Ile Pro Leu Val Leu Gly Thr Cys Lys Glu Thr Phe
    105                 110                 115

AAT CTG TAT TAC ATG GAA TCC GAT GAT GAC CAT TTG GCA AAG TTC AGA        436
Asn Leu Tyr Tyr Met Glu Ser Asp Asp Asp His Leu Ala Lys Phe Arg
120                 125                 130                 135

GAG CAC CAA TTT ACG AAG ATT GAC ACC ATG GCG GCT GAT GAG AGC TTC        484
Glu His Gln Phe Thr Lys Ile Asp Thr Met Ala Ala Asp Glu Ser Phe
                140                 145                 150

ACC CAG ATG GAT CTT GGG GAC CGG ATT CTC AAG CTG AAT ACC GAA GTC        532
Thr Gln Met Asp Leu Gly Asp Arg Ile Leu Lys Leu Asn Thr Glu Val
            155                 160                 165

CGC GAG GTG GGA CCT GTT AGT AAG AAG GGC TTT TAC TTG GCT TTC CAA        580
Arg Glu Val Gly Pro Val Ser Lys Lys Gly Phe Tyr Leu Ala Phe Gln
        170                 175                 180

GAT GTA GGT GCA TGT GTT GCC TTA GTC TCG GTG CGA GTG TAC TTC AAG        628
Asp Val Gly Ala Cys Val Ala Leu Val Ser Val Arg Val Tyr Phe Lys
    185                 190                 195

AAG TGC CCT TTC ACT GTC AAG AAC CTC GCC ATG TTT CCA GAT ACA GTT        676
Lys Cys Pro Phe Thr Val Lys Asn Leu Ala Met Phe Pro Asp Thr Val
200                 205                 210                 215

CCT ATG GAC TCC CAG TCC CTG GTG GAG GTG CGG GGT TCT TGT GTC AAT        724
Pro Met Asp Ser Gln Ser Leu Val Glu Val Arg Gly Ser Cys Val Asn
                220                 225                 230

CAT TCC AAG GAG GAA GAG CCA CCC AAG ATG TAC TGC AGC ACG GAA GGA        772
His Ser Lys Glu Glu Glu Pro Pro Lys Met Tyr Cys Ser Thr Glu Gly
            235                 240                 245

GAA TGG CTA GTG CCC ATA GGG AAG TGC TTG TGT AAT GCT GGC TAT GAA        820
Glu Trp Leu Val Pro Ile Gly Lys Cys Leu Cys Asn Ala Gly Tyr Glu
        250                 255                 260

GAG AGA GGC TTT GCG TGC CAA GCT TGT CGA CCT GGG TTC TAT AAA GCT        868
Glu Arg Gly Phe Ala Cys Gln Ala Cys Arg Pro Gly Phe Tyr Lys Ala
    265                 270                 275

TCT GCT GGC AAT GTG AAG TGT GCC AAA TGC CCA CCT CAC AGC TCT ACC        916
Ser Ala Gly Asn Val Lys Cys Ala Lys Cys Pro Pro His Ser Ser Thr
280                 285                 290                 295

TAT GAA GAT GCA TCT CTG AAC TGC AGG TGT GAA AAG AAT TAC TTT CGC        964
Tyr Glu Asp Ala Ser Leu Asn Cys Arg Cys Glu Lys Asn Tyr Phe Arg
                300                 305                 310

TCT GAG AAA GAC CCT CCA TCC ATG GCT TGC ACC AGA CCA CCA TCT GCT       1012
Ser Glu Lys Asp Pro Pro Ser Met Ala Cys Thr Arg Pro Pro Ser Ala
            315                 320                 325
```

```
CCA AGA AAC GTT ATT TCT AAC ATC AAT GAG ACA TCT GTT ATT CTG GAC      1060
Pro Arg Asn Val Ile Ser Asn Ile Asn Glu Thr Ser Val Ile Leu Asp
        330                 335                 340

TGG AGC TGG CCT CTT GAT ACA GGA GGT CGA AAA GAT GTC ACT TTC AAC      1108
Trp Ser Trp Pro Leu Asp Thr Gly Gly Arg Lys Asp Val Thr Phe Asn
    345                 350                 355

ATC ATT TGC AAA AAA TGT GGA GGA AGC AGC AAG ATA TGT GAG CCT TGC      1156
Ile Ile Cys Lys Lys Cys Gly Gly Ser Ser Lys Ile Cys Glu Pro Cys
360                 365                 370                 375

AGT GAC AAC GTA CGG TTC TTA CCC CGT CAG ACT GGC CTC ACC AAC ACC      1204
Ser Asp Asn Val Arg Phe Leu Pro Arg Gln Thr Gly Leu Thr Asn Thr
                380                 385                 390

ACG GTG ACA GTA GTG GAC CTT TTG GCA CAT ACC AAT TAC ACT TTT GAG      1252
Thr Val Thr Val Val Asp Leu Leu Ala His Thr Asn Tyr Thr Phe Glu
            395                 400                 405

ATT GAT GCA GTC AAC GGG GTA TCT GAC TTG AGT ACA CTT TCG AGA CAA      1300
Ile Asp Ala Val Asn Gly Val Ser Asp Leu Ser Thr Leu Ser Arg Gln
        410                 415                 420

TTT GCT GCT GTC AGC ATC ACG ACT AAT CAG GCT GCG CCA TCC CCC ATC      1348
Phe Ala Ala Val Ser Ile Thr Thr Asn Gln Ala Ala Pro Ser Pro Ile
    425                 430                 435

ACA GTG ATA AGG AAC GAC CGG ACA TCC AGG AAC AGC GTG TCT CTG TCT      1396
Thr Val Ile Arg Asn Asp Arg Thr Ser Arg Asn Ser Val Ser Leu Ser
440                 445                 450                 455

TGG CAG GAG CCT GAG CAC CCA AAT GGA ATC ATC TTG GAC TAC GAG GTC      1444
Trp Gln Glu Pro Glu His Pro Asn Gly Ile Ile Leu Asp Tyr Glu Val
                460                 465                 470

AAA TAC TAC GAA AAG CAG GAA CAA GAG ACA AGC TAT ACT ATT CTG AGA      1492
Lys Tyr Tyr Glu Lys Gln Glu Gln Glu Thr Ser Tyr Thr Ile Leu Arg
            475                 480                 485

GCC AAA AGC ACT AAC GTT ACT ATC AGC GGC CTC AAA CCT GAT ACC ACC      1540
Ala Lys Ser Thr Asn Val Thr Ile Ser Gly Leu Lys Pro Asp Thr Thr
        490                 495                 500

TAC GTC TTC CAA ATT CGA GCC CGA ACT GCA GCT AGA TAT GGG ACA AGC      1588
Tyr Val Phe Gln Ile Arg Ala Arg Thr Ala Ala Arg Tyr Gly Thr Ser
    505                 510                 515

AGC CGC AAG TTT GAA TTT GAA ACC AGT CCA GAT TCA TTC TCC ATT TCC      1636
Ser Arg Lys Phe Glu Phe Glu Thr Ser Pro Asp Ser Phe Ser Ile Ser
520                 525                 530                 535

AGT GAA AAT AGC CAG GTC GTT ATG ATT GCC ATT TCA GCT GCA GTT GCC      1684
Ser Glu Asn Ser Gln Val Val Met Ile Ala Ile Ser Ala Ala Val Ala
                540                 545                 550

ATC ATT CTC CTC ACG GTT GTT GTG TAC GTC TTG ATT GGG AGA TTC TGC      1732
Ile Ile Leu Leu Thr Val Val Val Tyr Val Leu Ile Gly Arg Phe Cys
            555                 560                 565

GGA TAC AAG AAG TCT AAA CAT GGT ACC GAT GAG AAA AGA CTA CAT TTT      1780
Gly Tyr Lys Lys Ser Lys His Gly Thr Asp Glu Lys Arg Leu His Phe
        570                 575                 580

GGG AAT GGC CAC TTA AAA CTC CCA GGC CTG AGA ACT TAT GTA GAT CCA      1828
Gly Asn Gly His Leu Lys Leu Pro Gly Leu Arg Thr Tyr Val Asp Pro
    585                 590                 595
```

```
CAT ACG TAC GAA GAT CCC AAT CAA GCT GTA CAT GAA TTT GCC AAG GAA      1876
His Thr Tyr Glu Asp Pro Asn Gln Ala Val His Glu Phe Ala Lys Glu
600                 605                 610                 615

CTA GAT GCT TCT AAT ATA TCA ATT GAT AAA GTT GTT GGA GCA GGG GAA      1924
Leu Asp Ala Ser Asn Ile Ser Ile Asp Lys Val Val Gly Ala Gly Glu
                620                 625                 630

TTT GGA GAA GTG TGC AGT GGG CGC CTG AAG CTG CCT TCT AAA AAG GAA      1972
Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Pro Ser Lys Lys Glu
            635                 640                 645

ATT TCA GTG GCC ATC AAA ACT CTG AAA GCT GGC TAC ACA GAA AAA CAG      2020
Ile Ser Val Ala Ile Lys Thr Leu Lys Ala Gly Tyr Thr Glu Lys Gln
        650                 655                 660

AGA AGG GAT TTC CTG GGA GAA GCA AGC ATC ATG GGG CAG TTT GAC CAC      2068
Arg Arg Asp Phe Leu Gly Glu Ala Ser Ile Met Gly Gln Phe Asp His
    665                 670                 675

CCC AAC ATC ATC CGA CTG GAG GGC GTT GTG ACT AAA AGT AAA CCA GTT      2116
Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr Lys Ser Lys Pro Val
680                 685                 690                 695

ATG ATT GTT ACT GAA TAC ATG GAA AAC GGT TCC TTG GAC AGC TTC CTA      2164
Met Ile Val Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Ser Phe Leu
                700                 705                 710

CGG AAA CAT GAT GCC CAG TTC ACA GTC ATT CAG CTA GTA GGC ATG CTT      2212
Arg Lys His Asp Ala Gln Phe Thr Val Ile Gln Leu Val Gly Met Leu
            715                 720                 725

CGT GGG ATC GCA TCT GGC ATG AAA TAT TTG TCA GAT ATG GGT TAT GTC      2260
Arg Gly Ile Ala Ser Gly Met Lys Tyr Leu Ser Asp Met Gly Tyr Val
        730                 735                 740

CAC CGA GAT CTA GCT GCT CGT AAT ATA CTC ATC AAT AGT AAC TTG GTG      2308
His Arg Asp Leu Ala Ala Arg Asn Ile Leu Ile Asn Ser Asn Leu Val
    745                 750                 755

TGC AAA GTC TCA GAT TTT GGT CTT TCT CGT GTA TTG GAA GAT GAC CCA      2356
Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu Asp Asp Pro
760                 765                 770                 775

GAA GCT GCT TAC ACA ACA AGG GGG GGC AAG ATT CCC ATC CGA TGG ACG      2404
Glu Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg Trp Thr
                780                 785                 790

TCA CCA GAA GCC ATT GCA TAC CGG AAG TTC ACA TCA GCC AGT GAT GCG      2452
Ser Pro Glu Ala Ile Ala Tyr Arg Lys Phe Thr Ser Ala Ser Asp Ala
            795                 800                 805

TGG AGC TAT GGG ATT GTC CTC TGG GAG GTG ATG TCT TAT GGA GAA AGG      2500
Trp Ser Tyr Gly Ile Val Leu Trp Glu Val Met Ser Tyr Gly Glu Arg
        810                 815                 820

CCG TAC TGG GAG ATG TCC TTC CAG GAC GTA ATT AAA GCC GTT GAT GAA      2548
Pro Tyr Trp Glu Met Ser Phe Gln Asp Val Ile Lys Ala Val Asp Glu
    825                 830                 835

GGG TAT CGC TTG CCA CCT CCT ATG GAC TGC CCA GCT GCC TTG TAT CAG      2596
Gly Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro Ala Ala Leu Tyr Gln
840                 845                 850                 855

CTG ATG CTG GAC TGC TGG CAG AAA GAC AGA AAC AAC AGA CCC AAG TTT      2644
Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Asn Arg Pro Lys Phe
                860                 865                 870
```

```
GAG CAG ATT GTC AGC ATC CTG GAT AAG CTG ATC CGT AAT CCC AGC AGT      2692
Glu Gln Ile Val Ser Ile Leu Asp Lys Leu Ile Arg Asn Pro Ser Ser
            875                 880                 885

CTG AAA ATA ATC ACC AAT GCG GCA GCA AGG CCA TCA AAT CTT CTC CTG      2740
Leu Lys Ile Ile Thr Asn Ala Ala Ala Arg Pro Ser Asn Leu Leu Leu
        890                 895                 900

GAC CAA AGT AAC ATT GAC ATT TCA GCG TTC CGC ACG GCA GGT GAT TGG      2788
Asp Gln Ser Asn Ile Asp Ile Ser Ala Phe Arg Thr Ala Gly Asp Trp
    905                 910                 915

CTC AAT GGT TTT CGA ACA GGA CAG TGC AAA GGC ATT TTC ACG GGT GTG      2836
Leu Asn Gly Phe Arg Thr Gly Gln Cys Lys Gly Ile Phe Thr Gly Val
920                 925                 930                 935

GAG TAC AGC TCC TGT GAT ACA ATA GCC AAG ATT TCC ACT GAT GAC ATG      2884
Glu Tyr Ser Ser Cys Asp Thr Ile Ala Lys Ile Ser Thr Asp Asp Met
                940                 945                 950

AAG AAA GTT GGT GTT ACA GTT GTG GGG CCT CAA AAG AAG ATT GTT AGC      2932
Lys Lys Val Gly Val Thr Val Val Gly Pro Gln Lys Lys Ile Val Ser
            955                 960                 965

AGT ATC AAA ACT CTA GAA ACT CAT ACG AAG AAC AGC CCT GTT CCT GTG      2980
Ser Ile Lys Thr Leu Glu Thr His Thr Lys Asn Ser Pro Val Pro Val
        970                 975                 980

TAAGGTACCA AAATGATGTT GCTGAGGACA GAAAAAAAAG AAAAGTCGCA TCAAAGTGCA    3040

AAAGCGATGG CTGATAAACG GCACGGTTTA AAGGAGTTCT TTGCAGCAGT TTTGGAAACA    3100

TAATGGTTGA AATTTCAAAC CCACTGAGAC ACTCAAATAC TGAGTATAAA TGCCTTAAAA    3160

ATAGGAGCGA ACTTGTTTTC TATCTGTTAA TCCTGAAGGG TGGGTGCTCT TAACTGACTG    3220

TTAATGCAGA TAGTAAATTT CAAAAAAAAA AACG                                3254
```

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 983 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

```
Met Asp Arg Arg Arg Leu Pro Leu Leu Leu Leu Cys Ala Ala Leu Gly
 1               5                  10                  15

Ser Ala Gly Arg Leu Ser Ala Arg Pro Gly Asn Glu Val Asn Leu Leu
            20                  25                  30

Asp Ser Lys Thr Ile Gln Gly Glu Leu Gly Trp Ile Ser Tyr Pro Ser
        35                  40                  45

His Gly Trp Glu Glu Ile Ser Gly Val Asp Glu His Tyr Thr Pro Ile
    50                  55                  60

Arg Thr Tyr Gln Glu Ser Asn Val Met Asp His Ser Gln Asn Asn Trp
65                  70                  75                  80

Leu Arg Thr Asn Trp Ile Pro Arg Asn Ser Ala Gln Lys Ile Tyr Val
                85                  90                  95
```

```
Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Ile Pro Leu Val Leu
            100                 105                 110

Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Met Glu Ser Asp Asp
        115                 120                 125

Asp His Leu Ala Lys Phe Arg Glu His Gln Phe Thr Lys Ile Asp Thr
    130                 135                 140

Met Ala Ala Asp Glu Ser Phe Thr Gln Met Asp Leu Gly Asp Arg Ile
145                 150                 155                 160

Leu Lys Leu Asn Thr Glu Val Arg Glu Val Gly Pro Val Ser Lys Lys
                165                 170                 175

Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Val Ala Leu Val
            180                 185                 190

Ser Val Arg Val Tyr Phe Lys Lys Cys Pro Phe Thr Val Lys Asn Leu
        195                 200                 205

Ala Met Phe Pro Asp Thr Val Pro Met Asp Ser Gln Ser Leu Val Glu
    210                 215                 220

Val Arg Gly Ser Cys Val Asn His Ser Lys Glu Glu Glu Pro Pro Lys
225                 230                 235                 240

Met Tyr Cys Ser Thr Glu Gly Glu Trp Leu Val Pro Ile Gly Lys Cys
                245                 250                 255

Leu Cys Asn Ala Gly Tyr Glu Glu Arg Gly Phe Ala Cys Gln Ala Cys
            260                 265                 270

Arg Pro Gly Phe Tyr Lys Ala Ser Ala Gly Asn Val Lys Cys Ala Lys
        275                 280                 285

Cys Pro Pro His Ser Ser Thr Tyr Glu Asp Ala Ser Leu Asn Cys Arg
    290                 295                 300

Cys Glu Lys Asn Tyr Phe Arg Ser Glu Lys Asp Pro Pro Ser Met Ala
305                 310                 315                 320

Cys Thr Arg Pro Pro Ser Ala Pro Arg Asn Val Ile Ser Asn Ile Asn
                325                 330                 335

Glu Thr Ser Val Ile Leu Asp Trp Ser Trp Pro Leu Asp Thr Gly Gly
            340                 345                 350

Arg Lys Asp Val Thr Phe Asn Ile Ile Cys Lys Lys Cys Gly Gly Ser
        355                 360                 365

Ser Lys Ile Cys Glu Pro Cys Ser Asp Asn Val Arg Phe Leu Pro Arg
    370                 375                 380

Gln Thr Gly Leu Thr Asn Thr Thr Val Thr Val Val Asp Leu Leu Ala
385                 390                 395                 400

His Thr Asn Tyr Thr Phe Glu Ile Asp Ala Val Asn Gly Val Ser Asp
                405                 410                 415

Leu Ser Thr Leu Ser Arg Gln Phe Ala Ala Val Ser Ile Thr Thr Asn
            420                 425                 430

Gln Ala Ala Pro Ser Pro Ile Thr Val Ile Arg Asn Asp Arg Thr Ser
        435                 440                 445
```

```
Arg Asn Ser Val Ser Leu Ser Trp Gln Glu Pro Glu His Pro Asn Gly
    450                 455                 460

Ile Ile Leu Asp Tyr Glu Val Lys Tyr Tyr Glu Lys Gln Glu Gln Glu
465                 470                 475                 480

Thr Ser Tyr Thr Ile Leu Arg Ala Lys Ser Thr Asn Val Thr Ile Ser
                485                 490                 495

Gly Leu Lys Pro Asp Thr Thr Tyr Val Phe Gln Ile Arg Ala Arg Thr
            500                 505                 510

Ala Ala Arg Tyr Gly Thr Ser Ser Arg Lys Phe Glu Phe Glu Thr Ser
        515                 520                 525

Pro Asp Ser Phe Ser Ile Ser Ser Glu Asn Ser Gln Val Val Met Ile
    530                 535                 540

Ala Ile Ser Ala Ala Val Ala Ile Ile Leu Leu Thr Val Val Val Tyr
545                 550                 555                 560

Val Leu Ile Gly Arg Phe Cys Gly Tyr Lys Lys Ser Lys His Gly Thr
                565                 570                 575

Asp Glu Lys Arg Leu His Phe Gly Asn Gly His Leu Lys Leu Pro Gly
            580                 585                 590

Leu Arg Thr Tyr Val Asp Pro His Thr Tyr Glu Asp Pro Asn Gln Ala
        595                 600                 605

Val His Glu Phe Ala Lys Glu Leu Asp Ala Ser Asn Ile Ser Ile Asp
    610                 615                 620

Lys Val Val Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu
625                 630                 635                 640

Lys Leu Pro Ser Lys Lys Glu Ile Ser Val Ala Ile Lys Thr Leu Lys
                645                 650                 655

Ala Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser
            660                 665                 670

Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val
        675                 680                 685

Val Thr Lys Ser Lys Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn
    690                 695                 700

Gly Ser Leu Asp Ser Phe Leu Arg Lys His Asp Ala Gln Phe Thr Val
705                 710                 715                 720

Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr
                725                 730                 735

Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile
            740                 745                 750

Leu Ile Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser
        755                 760                 765

Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly
    770                 775                 780

Lys Ile Pro Ile Arg Trp Thr Ser Pro Glu Ala Ile Ala Tyr Arg Lys
785                 790                 795                 800
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Phe Thr Ser Ala Ser Asp Ala Trp Ser Tyr Gly Ile Val Leu Trp Glu
                805                 810                 815

Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Glu Met Ser Phe Gln Asp
            820                 825                 830

Val Ile Lys Ala Val Asp Glu Gly Tyr Arg Leu Pro Pro Pro Met Asp
        835                 840                 845

Cys Pro Ala Ala Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp
    850                 855                 860

Arg Asn Asn Arg Pro Lys Phe Glu Gln Ile Val Ser Ile Leu Asp Lys
865                 870                 875                 880

Leu Ile Arg Asn Pro Ser Ser Leu Lys Ile Ile Thr Asn Ala Ala Ala
                885                 890                 895

Arg Pro Ser Asn Leu Leu Leu Asp Gln Ser Asn Ile Asp Ile Ser Ala
            900                 905                 910

Phe Arg Thr Ala Gly Asp Trp Leu Asn Gly Phe Arg Thr Gly Gln Cys
        915                 920                 925

Lys Gly Ile Phe Thr Gly Val Glu Tyr Ser Ser Cys Asp Thr Ile Ala
    930                 935                 940

Lys Ile Ser Thr Asp Asp Met Lys Lys Val Gly Val Thr Val Val Gly
945                 950                 955                 960

Pro Gln Lys Lys Ile Val Ser Ser Ile Lys Thr Leu Glu Thr His Thr
                965                 970                 975

Lys Asn Ser Pro Val Pro Val
            980
```

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4049 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 10..2994

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

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CGGCTTCTG ATG CCC GGC CCG GAG CGC ACC ATG GGG CCG TTG TGG TTC          48
          Met Pro Gly Pro Glu Arg Thr Met Gly Pro Leu Trp Phe
            1               5                  10

TGC TGT TTG CCC CTC GCC CTC TTG CCT CTG CTC GCC GCC GTG GAA GAG        96
Cys Cys Leu Pro Leu Ala Leu Leu Pro Leu Leu Ala Ala Val Glu Glu
     15                  20                  25

ACG CTG ATG GAC TCC ACA ACG GCC ACA GCA GAG CTG GGC TGG ATG GTG       144
Thr Leu Met Asp Ser Thr Thr Ala Thr Ala Glu Leu Gly Trp Met Val
 30                  35                  40                  45

CAT CCT CCC TCA GGG TGG GAA GAG GTG AGT GGA TAC GAT GAG AAC ATG       192
His Pro Pro Ser Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Asn Met
                 50                  55                  60
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AAC ACC ATC CGC ACC TAC CAG GTG TGC AAC GTC TTT GAA TCC AGC CAA        240
Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Ser Ser Gln
                65                  70                  75

AAC AAC TGG CTG CGG ACC AAG TAC ATC CGG AGG CGA GGA GCG CAC CGC        288
Asn Asn Trp Leu Arg Thr Lys Tyr Ile Arg Arg Arg Gly Ala His Arg
         80                  85                  90

ATC CAC GTG GAG ATG AAA TTC TCC GTT CGG GAC TGC AGC AGC ATC CCC        336
Ile His Val Glu Met Lys Phe Ser Val Arg Asp Cys Ser Ser Ile Pro
     95                 100                 105

AAC GTC CCG GGC TCC TGT AAG GAG ACT TTT AAC CTC TAT TAC TAC GAA        384
Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu
110                 115                 120                 125

TCA GAC TTT GAC TCT GCC ACC AAG ACT TTT CCT AAC TGG ATG GAA AAC        432
Ser Asp Phe Asp Ser Ala Thr Lys Thr Phe Pro Asn Trp Met Glu Asn
                130                 135                 140

CCT TGG ATG AAG GTA GAT ACA ATT GCT GCC GAC GAG AGC TTC TCG CAG        480
Pro Trp Met Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser Gln
            145                 150                 155

GTG GAC CTT GGT GGG CGG GTG ATG AAG ATT AAC ACC GAG GTG CGC AGT        528
Val Asp Leu Gly Gly Arg Val Met Lys Ile Asn Thr Glu Val Arg Ser
        160                 165                 170

TTT GGG CCT GTC TCC AAA AAC GGT TTC TAC CTG GCC TTC CAG GAC TAC        576
Phe Gly Pro Val Ser Lys Asn Gly Phe Tyr Leu Ala Phe Gln Asp Tyr
    175                 180                 185

GGG GGC TGC ATG TCC TTG ATT GCA GTC CGT GTC TTT TAC CGC AAG TGT        624
Gly Gly Cys Met Ser Leu Ile Ala Val Arg Val Phe Tyr Arg Lys Cys
190                 195                 200                 205

CCC CGT GTG ATC CAG AAC GGG GCG GTC TTC CAG GAA ACC CTC TCG GGA        672
Pro Arg Val Ile Gln Asn Gly Ala Val Phe Gln Glu Thr Leu Ser Gly
                210                 215                 220

GCG GAG AGC ACA TCT CTG GTG GCA GCC CGG GGG ACG TGC ATC AGC AAT        720
Ala Glu Ser Thr Ser Leu Val Ala Ala Arg Gly Thr Cys Ile Ser Asn
            225                 230                 235

GCG GAG GAG GTG GAT GTG CCC ATC AAG CTG TAC TGC AAT GGG GAT GGC        768
Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly Asp Gly
        240                 245                 250

GAG TGG CTG GTG CCC ATC GGC CGC TGC ATG TGC AGG CCG GGC TAT GAG        816
Glu Trp Leu Val Pro Ile Gly Arg Cys Met Cys Arg Pro Gly Tyr Glu
    255                 260                 265

TCG GTG GAG AAT GGG ACC GTC TGC AGA GGC TGC CCA TCA GGG ACC TTC        864
Ser Val Glu Asn Gly Thr Val Cys Arg Gly Cys Pro Ser Gly Thr Phe
270                 275                 280                 285

AAG GCC AGC CAA GGA GAT GAA GGA TGT GTC CAT TGT CCA ATT AAC AGC        912
Lys Ala Ser Gln Gly Asp Glu Gly Cys Val His Cys Pro Ile Asn Ser
                290                 295                 300

CGG ACG ACT TCG GAA GGG GCC ACG AAC TGC GTG TGC CGA AAC GGA TAT        960
Arg Thr Thr Ser Glu Gly Ala Thr Asn Cys Val Cys Arg Asn Gly Tyr
            305                 310                 315

TAC CGG GCA GAT GCT GAC CCC GTC GAC ATG CCA TGC ACC ACC ATC CCA       1008
Tyr Arg Ala Asp Ala Asp Pro Val Asp Met Pro Cys Thr Thr Ile Pro
        320                 325                 330
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TCT GCC CCC CAG GCC GTG ATC TCC AGC GTG AAT GAA ACC TCC CTG ATG      1056
Ser Ala Pro Gln Ala Val Ile Ser Ser Val Asn Glu Thr Ser Leu Met
    335                 340                 345

CTG GAG TGG ACC CCA CCA CGA GAC TCA GGG GGC CGG GAG GAT CTG GTA      1104
Leu Glu Trp Thr Pro Pro Arg Asp Ser Gly Gly Arg Glu Asp Leu Val
350                 355                 360                 365

TAC AAC ATC ATC TGC AAG AGC TGT GGG TCA GGC CGT GGG GCG TGC ACG      1152
Tyr Asn Ile Ile Cys Lys Ser Cys Gly Ser Gly Arg Gly Ala Cys Thr
                370                 375                 380

CGC TGT GGG GAC AAC GTG CAG TTT GCC CCA CGC CAG CTG GGC CTG ACG      1200
Arg Cys Gly Asp Asn Val Gln Phe Ala Pro Arg Gln Leu Gly Leu Thr
            385                 390                 395

GAG CCT CGC ATC TAC ATC AGC GAC CTG CTG GCC CAC ACG CAG TAC ACC      1248
Glu Pro Arg Ile Tyr Ile Ser Asp Leu Leu Ala His Thr Gln Tyr Thr
        400                 405                 410

TTT GAG ATC CAG GCT GTG AAT GGG GTC ACC GAC CAG AGC CCC TTC TCC      1296
Phe Glu Ile Gln Ala Val Asn Gly Val Thr Asp Gln Ser Pro Phe Ser
    415                 420                 425

CCA CAG TTT GCA TCA GTG AAT ATC ACC ACC AAC CAG GCT GCT CCT TCA      1344
Pro Gln Phe Ala Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser
430                 435                 440                 445

GCC GTG TCC ATA ATG CAC CAG GTC AGC CGC ACT GTG GAC AGC ATT ACC      1392
Ala Val Ser Ile Met His Gln Val Ser Arg Thr Val Asp Ser Ile Thr
                450                 455                 460

CTC TCG TGG TCT CAA CCT GAC CAG CCC AAT GGA GTC ATC CTG GAT TAT      1440
Leu Ser Trp Ser Gln Pro Asp Gln Pro Asn Gly Val Ile Leu Asp Tyr
            465                 470                 475

GAG CTG CAA TAC TAT GAG AAG AAC CTG AGT GAG TTA AAT TCA ACA GCA      1488
Glu Leu Gln Tyr Tyr Glu Lys Asn Leu Ser Glu Leu Asn Ser Thr Ala
        480                 485                 490

GTG AAG AGC CCC ACC AAC ACT GTG ACA GTG CAA AAC CTC AAA GCT GGC      1536
Val Lys Ser Pro Thr Asn Thr Val Thr Val Gln Asn Leu Lys Ala Gly
    495                 500                 505

ACC ATC TAT GTC TTC CAA GTG CGA GCA CGT ACC GTG GCT GGG TAT GGC      1584
Thr Ile Tyr Val Phe Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly
510                 515                 520                 525

CGG TAT AGT GGC AAG ATG TAC TTC CAG ACC ATG ACT GAA GCC GAG TAC      1632
Arg Tyr Ser Gly Lys Met Tyr Phe Gln Thr Met Thr Glu Ala Glu Tyr
                530                 535                 540

CAG ACC AGT GTC CAG GAG AAG CTG CCA CTC ATC ATT GGC TCC TCT GCA      1680
Gln Thr Ser Val Gln Glu Lys Leu Pro Leu Ile Ile Gly Ser Ser Ala
            545                 550                 555

GCA GGA CTG GTG TTT CTC ATT GCT GTT GTC GTC ATC ATT ATT GTC TGC      1728
Ala Gly Leu Val Phe Leu Ile Ala Val Val Val Ile Ile Ile Val Cys
        560                 565                 570

AAC AGA AGA CGG GGC TTT GAA CGT GCT GAC TCT GAG TAC ACT GAC AAG      1776
Asn Arg Arg Arg Gly Phe Glu Arg Ala Asp Ser Glu Tyr Thr Asp Lys
    575                 580                 585

CTG CAG CAC TAT ACC AGT GGC CAC ATG ACT CCA GGG ATG AAG ATT TAT      1824
Leu Gln His Tyr Thr Ser Gly His Met Thr Pro Gly Met Lys Ile Tyr
590                 595                 600                 605
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ATC GAT CCA TTT ACC TAC GAA GAT CCC AAT GAG GCT GTC AGG GAA TTT      1872
Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe
                610                 615                 620

GCA AAA GAA ATT GAT ATC TCC TGT GTG AAA ATC GAG CAG GTG ATT GGG      1920
Ala Lys Glu Ile Asp Ile Ser Cys Val Lys Ile Glu Gln Val Ile Gly
            625                 630                 635

GCA GGG GAG TTT GGT GAG GTG TGC AGT GGG CAT CTC AAG CTT CCT GGC      1968
Ala Gly Glu Phe Gly Glu Val Cys Ser Gly His Leu Lys Leu Pro Gly
        640                 645                 650

AAA AGA GAG ATC TTT GTG GCC ATC AAG ACC CTG AAG TCT GGT TAC ACA      2016
Lys Arg Glu Ile Phe Val Ala Ile Lys Thr Leu Lys Ser Gly Tyr Thr
    655                 660                 665

GAG AAG CAG AGA CGG GAC TTC CTG AGT GAA GCC AGC ATC ATG GGG CAG      2064
Glu Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln
670                 675                 680                 685

TTT GAC CAC CCC AAT GTC ATC CAC CTG GAA GGG GTG GTG ACC AAG AGT      2112
Phe Asp His Pro Asn Val Ile His Leu Glu Gly Val Val Thr Lys Ser
                690                 695                 700

TCC CCA GTC ATG ATC ATT ACA GAG TTC ATG GAG AAT GGC TCG TTG GAC      2160
Ser Pro Val Met Ile Ile Thr Glu Phe Met Glu Asn Gly Ser Leu Asp
            705                 710                 715

TCC TTC TTG AGG CAA AAT GAT GGG CAG TTC ACA GTG ATC CAG CTG GTG      2208
Ser Phe Leu Arg Gln Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val
        720                 725                 730

GGC ATG TTG CGT GGC ATT GCA GCA GGC ATG AAG TAC CTG GCT GAT ATG      2256
Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala Asp Met
    735                 740                 745

AAC TAC GTG CAC CGG GAC CTG GCT GCC CGC AAC ATC CTG GTC AAC AGC      2304
Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser
750                 755                 760                 765

AAC CTG GTC TGC AAG GTG TCC GAC TTC GGC CTC TCC CGT TTC CTG GAG      2352
Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu
                770                 775                 780

GAT GAC ACC TCT GAT CCC ACT TAC ACC AGC GCA CTG GGT GGA AAG ATC      2400
Asp Asp Thr Ser Asp Pro Thr Tyr Thr Ser Ala Leu Gly Gly Lys Ile
            785                 790                 795

CCA ATA CGG TGG ACA GCG CCT GAG GCA ATT CAG TAC CGA AAA TTC ACA      2448
Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr
        800                 805                 810

TCA GCC AGC GAT GTG TGG AGC TAT GGA ATA GTC ATG TGG GAG GTG ATG      2496
Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met
    815                 820                 825

TCG TAC GGC GAG CGG CCT TAC TGG GAC ATG ACC AAT CAA GAT GTG ATA      2544
Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Thr Asn Gln Asp Val Ile
830                 835                 840                 845

AAT GCT ATT GAG CAG GAC TAT CGG CTA CCA CCC CCT ATG GAT TGT CCA      2592
Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro
                850                 855                 860

AAT GCC CTG CAC CAG CTA ATG CTT GAC TGC TGG CAG AAG GAT CGA AAC      2640
Asn Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn
            865                 870                 875
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CAC AGA CCC AAA TTT GGA CAG ATT GTC AAC ACT TTA GAC AAA ATG ATC      2688
His Arg Pro Lys Phe Gly Gln Ile Val Asn Thr Leu Asp Lys Met Ile
        880                 885                 890

CGA AAT CCT AAT AGT CTG AAA GCC ATG GCA CCT CTC TCC TCT GGG GTT      2736
Arg Asn Pro Asn Ser Leu Lys Ala Met Ala Pro Leu Ser Ser Gly Val
    895                 900                 905

AAC CTC CCT CTA CTT GAC CGC ACA ATC CCA GAT TAT ACC AGC TTC AAC      2784
Asn Leu Pro Leu Leu Asp Arg Thr Ile Pro Asp Tyr Thr Ser Phe Asn
910                 915                 920                 925

ACT GTG GAT GAA TGG CTG GAT GCC ATC AAG ATG AGC CAG TAC AAG GAG      2832
Thr Val Asp Glu Trp Leu Asp Ala Ile Lys Met Ser Gln Tyr Lys Glu
                930                 935                 940

AGC TTT GCC AGT GCT GGC TTC ACC ACC TTT GAT ATA GTA TCT CAG ATG      2880
Ser Phe Ala Ser Ala Gly Phe Thr Thr Phe Asp Ile Val Ser Gln Met
            945                 950                 955

ACT GTA GAG GAC ATT CTA CGA GTT GGG GTC ACT TTA GCA GGA CAC CAG      2928
Thr Val Glu Asp Ile Leu Arg Val Gly Val Thr Leu Ala Gly His Gln
        960                 965                 970

AAG AAA ATT CTG AAC AGT ATC CAG GTG ATG AGA GCA CAG ATG AAC CAA      2976
Lys Lys Ile Leu Asn Ser Ile Gln Val Met Arg Ala Gln Met Asn Gln
    975                 980                 985

ATT CAG TCT GTG GAG GTT TGATAGCAAC ACGTCCTCGT GCTCCACTTC             3024
Ile Gln Ser Val Glu Val
990                 995

CTTGAGGCCC TGCTCCCCTC TGCCCCTGTG TGTCTGAGCT CCAGTTCTTG AGTGTTCTGC    3084

GTGGATCAGA GACAGGCAGC TGCTCTGAGG ATCATGGCAA CAGGAAGAAA TGCCCTATCA    3144

TTGACAACGA GAAGTCATCA AGAGGTGAAA CAATGGAAAA CAATGGAAAA AGGGAACAAG    3204

TAAAGACAGC TATTTTGAAA ACCGAAAACA AACAGTGAAT TATTTTTAAA TAATAATAAA    3264

GCAATTGCAG TCTTGAAAAG GGCTCCAAGA CCAATGGGAG TCTCCAAAGG AAGAGAATAG    3324

AGCAGCTTCA TCTATTTCCT CTTACACAAG GGTTGCTGCA GCTGGGCCCA GACACTTCTG    3384

GAGTAACGAG ACTTTTCAAG AAGATGAATG CAAAGAATGG TCACAAGAAG CACTTCTCTT    3444

TCTCACATGG GATGGCAGCT CTGGGAATGC CCGGCAGTCC TTCCTGAAAG CCCTGTTGGC    3504

AAATCGAAGA GGAGAGCCGA AGCTCTTTGG TGCTGTGGAA CCAAGTGCAT CTCAGAAATT    3564

GTTGGACTTC TACAAAAGCT GAAGACATTC TTTTTTTTTA AACAAGTAAA CTGATACTAG    3624

AAGAGGCTGT TTCCGTCAAA TGAGAAGGAA TCTGTAACAC TGGCCCGGGG GGGGTGGGGA    3684

ATGGGGGAAA TCAGTCCTTT TTACATCTCT TTATTTTCTC TTGTCATGGA ACAGTTTTGT    3744

GAGTGACAGT TTCCTAAGGG TCCGTCCATC CACCCTCCAA TGGCATCATT GTTTCATACA    3804

TATCATATGC ACAAGACTTA TAGTGATGTC CTCACTCGAT GCCAATGATC TTTCCCCAGA    3864

AGACTTCCCA AGTACAGTAT GTAGTAGATT TTGATTACAA ATGCTGACGT GTACCTTTAT    3924

TTTTCGGTTG TCGTTGTTGG GAGATTCGTC CTTTTACCTT GCTTTGTTAA CACCAATTTG    3984

TGAGTTTGGG GTTGGAATTT TTTTGGTCGA TTGGGGTTGT TTTTTTTTTT TTTTTTTTTT    4044

AACCG                                                                4049
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(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 995 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

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Met Pro Gly Pro Glu Arg Thr Met Gly Pro Leu Trp Phe Cys Cys Leu
 1               5                  10                  15

Pro Leu Ala Leu Leu Pro Leu Leu Ala Ala Val Glu Glu Thr Leu Met
            20                  25                  30

Asp Ser Thr Thr Ala Thr Ala Glu Leu Gly Trp Met Val His Pro Pro
        35                  40                  45

Ser Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Asn Met Asn Thr Ile
    50                  55                  60

Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Ser Ser Gln Asn Asn Trp
65                  70                  75                  80

Leu Arg Thr Lys Tyr Ile Arg Arg Arg Gly Ala His Arg Ile His Val
                85                  90                  95

Glu Met Lys Phe Ser Val Arg Asp Cys Ser Ser Ile Pro Asn Val Pro
            100                 105                 110

Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu Ser Asp Phe
        115                 120                 125

Asp Ser Ala Thr Lys Thr Phe Pro Asn Trp Met Glu Asn Pro Trp Met
    130                 135                 140

Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser Gln Val Asp Leu
145                 150                 155                 160

Gly Gly Arg Val Met Lys Ile Asn Thr Glu Val Arg Ser Phe Gly Pro
                165                 170                 175

Val Ser Lys Asn Gly Phe Tyr Leu Ala Phe Gln Asp Tyr Gly Gly Cys
            180                 185                 190

Met Ser Leu Ile Ala Val Arg Val Phe Tyr Arg Lys Cys Pro Arg Val
        195                 200                 205

Ile Gln Asn Gly Ala Val Phe Gln Glu Thr Leu Ser Gly Ala Glu Ser
    210                 215                 220

Thr Ser Leu Val Ala Ala Arg Gly Thr Cys Ile Ser Asn Ala Glu Glu
225                 230                 235                 240

Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly Asp Gly Glu Trp Leu
                245                 250                 255

Val Pro Ile Gly Arg Cys Met Cys Arg Pro Gly Tyr Glu Ser Val Glu
            260                 265                 270

Asn Gly Thr Val Cys Arg Gly Cys Pro Ser Gly Thr Phe Lys Ala Ser
        275                 280                 285
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Gln Gly Asp Glu Gly Cys Val His Cys Pro Ile Asn Ser Arg Thr Thr
    290                 295                 300

Ser Glu Gly Ala Thr Asn Cys Val Cys Arg Asn Gly Tyr Tyr Arg Ala
305                 310                 315                 320

Asp Ala Asp Pro Val Asp Met Pro Cys Thr Thr Ile Pro Ser Ala Pro
                325                 330                 335

Gln Ala Val Ile Ser Ser Val Asn Glu Thr Ser Leu Met Leu Glu Trp
            340                 345                 350

Thr Pro Pro Arg Asp Ser Gly Gly Arg Glu Asp Leu Val Tyr Asn Ile
        355                 360                 365

Ile Cys Lys Ser Cys Gly Ser Gly Arg Gly Ala Cys Thr Arg Cys Gly
    370                 375                 380

Asp Asn Val Gln Phe Ala Pro Arg Gln Leu Gly Leu Thr Glu Pro Arg
385                 390                 395                 400

Ile Tyr Ile Ser Asp Leu Leu Ala His Thr Gln Tyr Thr Phe Glu Ile
                405                 410                 415

Gln Ala Val Asn Gly Val Thr Asp Gln Ser Pro Phe Ser Pro Gln Phe
            420                 425                 430

Ala Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Ala Val Ser
        435                 440                 445

Ile Met His Gln Val Ser Arg Thr Val Asp Ser Ile Thr Leu Ser Trp
    450                 455                 460

Ser Gln Pro Asp Gln Pro Asn Gly Val Ile Leu Asp Tyr Glu Leu Gln
465                 470                 475                 480

Tyr Tyr Glu Lys Asn Leu Ser Glu Leu Asn Ser Thr Ala Val Lys Ser
                485                 490                 495

Pro Thr Asn Thr Val Thr Val Gln Asn Leu Lys Ala Gly Thr Ile Tyr
            500                 505                 510

Val Phe Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly Arg Tyr Ser
        515                 520                 525

Gly Lys Met Tyr Phe Gln Thr Met Thr Glu Ala Glu Tyr Gln Thr Ser
    530                 535                 540

Val Gln Glu Lys Leu Pro Leu Ile Ile Gly Ser Ser Ala Ala Gly Leu
545                 550                 555                 560

Val Phe Leu Ile Ala Val Val Val Ile Ile Ile Val Cys Asn Arg Arg
                565                 570                 575

Arg Gly Phe Glu Arg Ala Asp Ser Glu Tyr Thr Asp Lys Leu Gln His
            580                 585                 590

Tyr Thr Ser Gly His Met Thr Pro Gly Met Lys Ile Tyr Ile Asp Pro
        595                 600                 605

Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe Ala Lys Glu
    610                 615                 620

Ile Asp Ile Ser Cys Val Lys Ile Glu Gln Val Ile Gly Ala Gly Glu
625                 630                 635                 640
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Phe Gly Glu Val Cys Ser Gly His Leu Lys Leu Pro Gly Lys Arg Glu
645 650 655

Ile Phe Val Ala Ile Lys Thr Leu Lys Ser Gly Tyr Thr Glu Lys Gln
660 665 670

Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Asp His
675 680 685

Pro Asn Val Ile His Leu Glu Gly Val Val Thr Lys Ser Ser Pro Val
690 695 700

Met Ile Ile Thr Glu Phe Met Glu Asn Gly Ser Leu Asp Ser Phe Leu
705 710 715 720

Arg Gln Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly Met Leu
725 730 735

Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala Asp Met Asn Tyr Val
740 745 750

His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val
755 760 765

Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu Asp Asp Thr
770 775 780

Ser Asp Pro Thr Tyr Thr Ser Ala Leu Gly Gly Lys Ile Pro Ile Arg
785 790 795 800

Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr Ser Ala Ser
805 810 815

Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly
820 825 830

Glu Arg Pro Tyr Trp Asp Met Thr Asn Gln Asp Val Ile Asn Ala Ile
835 840 845

Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro Asn Ala Leu
850 855 860

His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn His Arg Pro
865 870 875 880

Lys Phe Gly Gln Ile Val Asn Thr Leu Asp Lys Met Ile Arg Asn Pro
885 890 895

Asn Ser Leu Lys Ala Met Ala Pro Leu Ser Ser Gly Val Asn Leu Pro
900 905 910

Leu Leu Asp Arg Thr Ile Pro Asp Tyr Thr Ser Phe Asn Thr Val Asp
915 920 925

Glu Trp Leu Asp Ala Ile Lys Met Ser Gln Tyr Lys Glu Ser Phe Ala
930 935 940

Ser Ala Gly Phe Thr Thr Phe Asp Ile Val Ser Gln Met Thr Val Glu
945 950 955 960

Asp Ile Leu Arg Val Gly Val Thr Leu Ala Gly His Gln Lys Lys Ile
965 970 975

Leu Asn Ser Ile Gln Val Met Arg Ala Gln Met Asn Gln Ile Gln Ser
980 985 990

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Val Glu Val
       995
```

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3125 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..2233

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

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C CTC AAA TTC ACC CTG AGG GAC TGT AAC AGC CTT CCA GGA GGA CTT          46
  Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu
    1               5                  10                  15

GGG ACT TGC AAG GAG ACT TTT AAC ATG TAC TAC TTT GAG TCA GAT GAT        94
Gly Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp
                20                  25                  30

GAA GAT GGG AGG AAC ATC AGA GAG AAT CAG TAC ATC AAG ATA GAT ACC       142
Glu Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr
            35                  40                  45

ATT GCT GCT GAT GAG AGC TTC ACG GAG TTG GAC CTC GGC GAC AGA GTT       190
Ile Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val
        50                  55                  60

ATG AAG TTA AAC ACA GAA GTG AGA GAT GTT GGG CCT CTA ACA AAA AAA       238
Met Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys
    65                  70                  75

GGA TTT TAC CTT GCT TTC CAG GAT GTG GGC GCC TGC ATT GCC CTG GTC       286
Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val
80                  85                  90                  95

TCT GTG CGT GTG TAC TAC AAG AAA TGC CCA TCA GTG ATC CGC AAC CTG       334
Ser Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu
                100                 105                 110

GCA CGC TTT CCA GAT ACC ATC ACA GGA GCA GAT TCC TCG CAG CTG CTA       382
Ala Arg Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu
            115                 120                 125

GAA GTG TCA GGC GTC TGT GTC AAC CAC TCA GTG ACT GAT GAG GCA CCA       430
Glu Val Ser Gly Val Cys Val Asn His Ser Val Thr Asp Glu Ala Pro
        130                 135                 140

AAG ATG CAC TGC AGT TCA GAG GGA GAA TGG CTG GTG CCC ATT GGG AAG       478
Lys Met His Cys Ser Ser Glu Gly Glu Trp Leu Val Pro Ile Gly Lys
    145                 150                 155

TGT TTG TGC AAG GCA GGG TAC GAG GAG AAG AAC AAC ACC TGC CAA GCA       526
Cys Leu Cys Lys Ala Gly Tyr Glu Glu Lys Asn Asn Thr Cys Gln Ala
160                 165                 170                 175

CCT TCT CCA GTC AGT AGT GTG AAA AAA GGG AAG ATA ACT AAA AAT AGC       574
Pro Ser Pro Val Ser Ser Val Lys Lys Gly Lys Ile Thr Lys Asn Ser
                180                 185                 190
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ATC TCC CTT TCC TGG CAG GAG CCA GAT CGA CCC AAC GGC ATC ATC CTG        622
Ile Ser Leu Ser Trp Gln Glu Pro Asp Arg Pro Asn Gly Ile Ile Leu
            195                 200                 205

GAA TAC GAA ATC AAA TAT TTT GAA AAG GAC CAG GAG ACA AGC TAC ACC        670
Glu Tyr Glu Ile Lys Tyr Phe Glu Lys Asp Gln Glu Thr Ser Tyr Thr
        210                 215                 220

ATC ATC AAA TCC AAA GAG ACC GCA ATT ACG GCA GAT GGC TTG AAA CCA        718
Ile Ile Lys Ser Lys Glu Thr Ala Ile Thr Ala Asp Gly Leu Lys Pro
    225                 230                 235

GGC TCA GCG TAC GTC TTC CAG ATC CGA GCC CGG ACA GCT GCT GGC TAC        766
Gly Ser Ala Tyr Val Phe Gln Ile Arg Ala Arg Thr Ala Ala Gly Tyr
240                 245                 250                 255

GGT GGC TTC AGT CGA AGA TTT GAG TTT GAA ACC AGC CCA GTG TTA GCT        814
Gly Gly Phe Ser Arg Arg Phe Glu Phe Glu Thr Ser Pro Val Leu Ala
                260                 265                 270

GCA TCC AGT GAC CAG AGC CAG ATT CCT ATA ATT GTT GTG TCT GTA ACA        862
Ala Ser Ser Asp Gln Ser Gln Ile Pro Ile Ile Val Val Ser Val Thr
            275                 280                 285

GTG GGA GTT ATT CTG CTG GCT GTT GTT ATC GGT TTC CTT CTC AGT GGA        910
Val Gly Val Ile Leu Leu Ala Val Val Ile Gly Phe Leu Leu Ser Gly
        290                 295                 300

AGT TGC TGC GAT CAT GGC TGT GGG TGG GCT TCT TCT CTG CGT GCT GTT        958
Ser Cys Cys Asp His Gly Cys Gly Trp Ala Ser Ser Leu Arg Ala Val
    305                 310                 315

GCC TAT CCG AGC CTA ATA TGG CGC TGT GGC TAC AGC AAG GCT AAA CAA       1006
Ala Tyr Pro Ser Leu Ile Trp Arg Cys Gly Tyr Ser Lys Ala Lys Gln
320                 325                 330                 335

GAC CCA GAA GAA GAA AAG ATG CAT TTT CAT AAT GGC CAC ATT AAA CTG       1054
Asp Pro Glu Glu Glu Lys Met His Phe His Asn Gly His Ile Lys Leu
                340                 345                 350

CCT GGT GTA AGA ACC TAC ATT GAT CCC CAC ACC TAT GAG GAC CCT AAT       1102
Pro Gly Val Arg Thr Tyr Ile Asp Pro His Thr Tyr Glu Asp Pro Asn
            355                 360                 365

CAA GCT GTC CAC GAG TTT GCC AAG GAA ATA GAA GCT TCG TGC ATA ACC       1150
Gln Ala Val His Glu Phe Ala Lys Glu Ile Glu Ala Ser Cys Ile Thr
        370                 375                 380

ATC GAG AGA GTT ATC GGA GCT GGT GAA TTT GGA GAA GTC TGC AGT GGA       1198
Ile Glu Arg Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly
    385                 390                 395

CGG CTG AAA CTG CAG GGA AAA CGC GAG TTT CCA GTG GCT ATC AAA ACC       1246
Arg Leu Lys Leu Gln Gly Lys Arg Glu Phe Pro Val Ala Ile Lys Thr
400                 405                 410                 415

CTG AAG GTG GGC TAC ACA GAG AAG CAA AGG CGA GAT TTC CTG GGA GAA       1294
Leu Lys Val Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Gly Glu
                420                 425                 430

GCG AGC ATC ATG GGG CAG TTC GAC CAC CCC AAC ATC ATC CAC CTG GAA       1342
Ala Ser Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His Leu Glu
            435                 440                 445

GGT GTC GTC ACA AAA AGC AAA CCT GTA ATG ATA GTA ACG GAA TAC ATG       1390
Gly Val Val Thr Lys Ser Lys Pro Val Met Ile Val Thr Glu Tyr Met
        450                 455                 460
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GAA AAT GGT TCT CTG GAT ACA TTT TTA AAG AAG AAC GAT GGG CAG TTC      1438
Glu Asn Gly Ser Leu Asp Thr Phe Leu Lys Lys Asn Asp Gly Gln Phe
    465                 470                 475

ACG GTC ATT CAG CTG GTC GGG ATG CTG CGA GGC ATC GCA TCA GGG ATG      1486
Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met
480                 485                 490                 495

AAG TAC CTG TCT GAC ATG GGT TAC GTA CAC AGA GAC CTC GCT GCC AGG      1534
Lys Tyr Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg
                500                 505                 510

AAT ATC CTC ATC AAC AGC AAC TTA GTC TGC AAG GTG TCT GAC TTT GGC      1582
Asn Ile Leu Ile Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly
            515                 520                 525

CTC TCC AGA GTC CTA GAA GAT GAT CCT GAA GCA GCG TAC ACA ACC AGG      1630
Leu Ser Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg
        530                 535                 540

GGA GGG AAG ATC CCC ATC CGA TGG ACG GCA CCT GAA GCA ATC GCC TTC      1678
Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe
    545                 550                 555

CGC AAA TTC ACG TCG GCC AGC GAT GTG TGG AGC TAC GGC ATT GTG ATG      1726
Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met
560                 565                 570                 575

TGG GAA GTG ATG TCC TAT GGC GAG AGA CCT TAC TGG GAA ATG ACA AAC      1774
Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Glu Met Thr Asn
                580                 585                 590

CAA GAT GTG ATT AAA GCC GTG GAG GAA GGC TAT CGC CTG CCA AGT CCC      1822
Gln Asp Val Ile Lys Ala Val Glu Glu Gly Tyr Arg Leu Pro Ser Pro
            595                 600                 605

ATG GAC TGC CCT GCT GCT CTC TAC CAG TTG ATG CTT GAC TGC TGG CAG      1870
Met Asp Cys Pro Ala Ala Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln
        610                 615                 620

AAA GAC CGC AAC AGC AGG CCC AAG TTT GAT GAA ATT GTC AGC ATG TTG      1918
Lys Asp Arg Asn Ser Arg Pro Lys Phe Asp Glu Ile Val Ser Met Leu
    625                 630                 635

GAC AAG CTC ATC CGT AAC CCA AGC AGC TTG AAG ACG TTG GTT AAT GCA      1966
Asp Lys Leu Ile Arg Asn Pro Ser Ser Leu Lys Thr Leu Val Asn Ala
640                 645                 650                 655

TCG AGC AGA GTA TCA AAT TTG TTG GTA GAA CAC AGT CCA GTG GGG AGC      2014
Ser Ser Arg Val Ser Asn Leu Leu Val Glu His Ser Pro Val Gly Ser
                660                 665                 670

GGT GCC TAC AGG TCA GTG GGT GAG TGG CTG GAA GCC ATC AAA ATG GGT      2062
Gly Ala Tyr Arg Ser Val Gly Glu Trp Leu Glu Ala Ile Lys Met Gly
            675                 680                 685

CGA TAC ACC GAG ATT TTC ATG GAG AAT GGA TAC AGT TCG ATG GAT TCT      2110
Arg Tyr Thr Glu Ile Phe Met Glu Asn Gly Tyr Ser Ser Met Asp Ser
        690                 695                 700

GTG GCT CAG GTG ACC CTA GAG GAT TTG AGG CGG CTG GGA GTG ACA CTT      2158
Val Ala Gln Val Thr Leu Glu Asp Leu Arg Arg Leu Gly Val Thr Leu
    705                 710                 715

GTT GGT CAC CAG AAG AAG ATA ATG AAC AGC CTT CAA GAG ATG AAG GTC      2206
Val Gly His Gln Lys Lys Ile Met Asn Ser Leu Gln Glu Met Lys Val
720                 725                 730                 735
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CAG TTG GTG AAT GGG ATG GTG CCA TTG TAACTCGGTT TTTAAGTCAC          2253
Gln Leu Val Asn Gly Met Val Pro Leu
                740

TTCCTCGAGT GGTCGGTCCT GCACTTTGTA TACTAGCTCT GAGATTTATT TTGACTAAAG  2313

AAGAAAAAAG GGAAATTCAG TGGTTTCTGT AACTGAAGGA CGCTGGCTTC TGCCACAGCA  2373

TTTATAAAGC AGTGTTTGAC TGAAGTTTTC ATTTTCTTCC TATTTGTGTC CTCATTCTCA  2433

TGAAGTAAAT GTAACATGCA TGGAACATGG AAATGGATCT ACTGTACATG AGGTTACCCA  2493

ATTTCTTGCG CTTCAGCATG ACAACAGCAA GCCTTCCCAC CACATGTTGT CTATACATGG  2553

GAGATATATA TATATGCATA TATATATATA GCACCTTTAT ATACTGAATT ACAGCAGCAG  2613

CACATGTTAA TACTTCCAAG GACTTACTTG ACTAGAGAAG TTTTGCAGCC ATTGTGGGCT  2673

CACACAAGCT GCGGTTTACT GAAGTTTACT TCAAGTCTTA CTTGTCTACA GAAGTGTATT  2733

GAAGAGCAAT ATGATTAGAT TATTTCTGGA TAGATATTTT GTTTTGTAAA TTTAAAAAAT  2793

CGTGTTACAC AGCGTTAAGT TATAGAGACT AGTGTATAAA CATGTTGCTT GCTCAATGGC  2853

AAATACAATA CAGGGTGTAT ATTTTTTTCT CTCTGTGTTG CAAAGTTCTT TTAGTTTGCT  2913

CTTCTGTGAG GATAATACGT TATGATGTAT ATACTGTACA GTTTGCTACA CATCAGGTAC  2973

AAGATTGGGG CTTTCTCAAT GTTTTGTTCT TTTTCCCTCT TTTGTTTCAT TTTGTCTTCC  3033

TTTTGTGTTA ACCACTATGC TTTGTATTTT TGCTGCTGTT TGGTTTGAGG CAACATATAA  3093

AGCTTTCAGG TGTTTTGATT ATAAAAAAAA AG                                 3125
```

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 744 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

```
Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu Gly
 1               5                  10                  15

Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp Glu
            20                  25                  30

Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr Ile
        35                  40                  45

Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val Met
    50                  55                  60

Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys Gly
65                  70                  75                  80

Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val Ser
                85                  90                  95

Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu Ala
            100                 105                 110
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Arg Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu Glu
        115                 120                 125

Val Ser Gly Val Cys Val Asn His Ser Val Thr Asp Glu Ala Pro Lys
    130                 135                 140

Met His Cys Ser Ser Glu Gly Glu Trp Leu Val Pro Ile Gly Lys Cys
145                 150                 155                 160

Leu Cys Lys Ala Gly Tyr Glu Glu Lys Asn Asn Thr Cys Gln Ala Pro
                165                 170                 175

Ser Pro Val Ser Ser Val Lys Lys Gly Lys Ile Thr Lys Asn Ser Ile
            180                 185                 190

Ser Leu Ser Trp Gln Glu Pro Asp Arg Pro Asn Gly Ile Ile Leu Glu
        195                 200                 205

Tyr Glu Ile Lys Tyr Phe Glu Lys Asp Gln Glu Thr Ser Tyr Thr Ile
    210                 215                 220

Ile Lys Ser Lys Glu Thr Ala Ile Thr Ala Asp Gly Leu Lys Pro Gly
225                 230                 235                 240

Ser Ala Tyr Val Phe Gln Ile Arg Ala Arg Thr Ala Ala Gly Tyr Gly
                245                 250                 255

Gly Phe Ser Arg Arg Phe Glu Phe Glu Thr Ser Pro Val Leu Ala Ala
            260                 265                 270

Ser Ser Asp Gln Ser Gln Ile Pro Ile Ile Val Val Ser Val Thr Val
        275                 280                 285

Gly Val Ile Leu Leu Ala Val Val Ile Gly Phe Leu Leu Ser Gly Ser
    290                 295                 300

Cys Cys Asp His Gly Cys Gly Trp Ala Ser Ser Leu Arg Ala Val Ala
305                 310                 315                 320

Tyr Pro Ser Leu Ile Trp Arg Cys Gly Tyr Ser Lys Ala Lys Gln Asp
                325                 330                 335

Pro Glu Glu Glu Lys Met His Phe His Asn Gly His Ile Lys Leu Pro
            340                 345                 350

Gly Val Arg Thr Tyr Ile Asp Pro His Thr Tyr Glu Asp Pro Asn Gln
        355                 360                 365

Ala Val His Glu Phe Ala Lys Glu Ile Glu Ala Ser Cys Ile Thr Ile
    370                 375                 380

Glu Arg Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg
385                 390                 395                 400

Leu Lys Leu Gln Gly Lys Arg Glu Phe Pro Val Ala Ile Lys Thr Leu
                405                 410                 415

Lys Val Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala
            420                 425                 430

Ser Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His Leu Glu Gly
        435                 440                 445

Val Val Thr Lys Ser Lys Pro Val Met Ile Val Thr Glu Tyr Met Glu
    450                 455                 460
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Asn Gly Ser Leu Asp Thr Phe Leu Lys Lys Asn Asp Gly Gln Phe Thr
465                 470                 475                 480

Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met Lys
                485                 490                 495

Tyr Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn
            500                 505                 510

Ile Leu Ile Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu
        515                 520                 525

Ser Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly
    530                 535                 540

Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg
545                 550                 555                 560

Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp
                565                 570                 575

Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Glu Met Thr Asn Gln
            580                 585                 590

Asp Val Ile Lys Ala Val Glu Glu Gly Tyr Arg Leu Pro Ser Pro Met
        595                 600                 605

Asp Cys Pro Ala Ala Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys
    610                 615                 620

Asp Arg Asn Ser Arg Pro Lys Phe Asp Glu Ile Val Ser Met Leu Asp
625                 630                 635                 640

Lys Leu Ile Arg Asn Pro Ser Ser Leu Lys Thr Leu Val Asn Ala Ser
                645                 650                 655

Ser Arg Val Ser Asn Leu Leu Val Glu His Ser Pro Val Gly Ser Gly
            660                 665                 670

Ala Tyr Arg Ser Val Gly Glu Trp Leu Glu Ala Ile Lys Met Gly Arg
        675                 680                 685

Tyr Thr Glu Ile Phe Met Glu Asn Gly Tyr Ser Ser Met Asp Ser Val
    690                 695                 700

Ala Gln Val Thr Leu Glu Asp Leu Arg Arg Leu Gly Val Thr Leu Val
705                 710                 715                 720

Gly His Gln Lys Lys Ile Met Asn Ser Leu Gln Glu Met Lys Val Gln
                725                 730                 735

Leu Val Asn Gly Met Val Pro Leu
            740
```

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3056 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: both
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..2131

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

```
C CTC AAA TTC ACC CTG AGG GAC TGT AAC AGC CTT CCA GGA GGA CTT          46
  Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu
    1               5                  10                  15

GGG ACT TGC AAG GAG ACT TTT AAC ATG TAC TAC TTT GAG TCA GAT GAT        94
Gly Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp
                20                  25                  30

GAA GAT GGG AGG AAC ATC AGA GAG AAT CAG TAC ATC AAG ATA GAT ACC       142
Glu Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr
            35                  40                  45

ATT GCT GCT GAT GAG AGC TTC ACG GAG TTG GAC CTC GGC GAC AGA GTT       190
Ile Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val
        50                  55                  60

ATG AAG TTA AAC ACA GAA GTG AGA GAT GTT GGG CCT CTA ACA AAA AAA       238
Met Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys
    65                  70                  75

GGA TTT TAC CTT GCT TTC CAG GAT GTG GGC GCC TGC ATT GCC CTG GTC       286
Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val
80                  85                  90                  95

TCT GTG CGT GTG TAC TAC AAG AAA TGC CCA TCA GTG ATC CGC AAC CTG       334
Ser Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu
                100                 105                 110

GCA CGC TTT CCA GAT ACC ATC ACA GGA GCA GAT TCC TCG CAG CTG CTA       382
Ala Arg Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu
            115                 120                 125

GAA GTG TCA GGC GTC TGT GTC AAC CAC TCA GTG ACT GAT GAG GCA CCA       430
Glu Val Ser Gly Val Cys Val Asn His Ser Val Thr Asp Glu Ala Pro
        130                 135                 140

AAG ATG CAC TGC AGT TCA GAG GGA GAA TGG CTG GTG CCC ATT GGG AAG       478
Lys Met His Cys Ser Ser Glu Gly Glu Trp Leu Val Pro Ile Gly Lys
    145                 150                 155

TGT TTG TGC AAG GCA GGG TAC GAG GAG AAG AAC AAC ACC TGC CAA GCA       526
Cys Leu Cys Lys Ala Gly Tyr Glu Glu Lys Asn Asn Thr Cys Gln Ala
160                 165                 170                 175

CCT TCT CCA GTC AGT AGT GTG AAA AAA GGG AAG ATA ACT AAA AAT AGC       574
Pro Ser Pro Val Ser Ser Val Lys Lys Gly Lys Ile Thr Lys Asn Ser
                180                 185                 190

ATC TCC CTT TCC TGG CAG GAG CCA GAT CGA CCC AAC GGC ATC ATC CTG       622
Ile Ser Leu Ser Trp Gln Glu Pro Asp Arg Pro Asn Gly Ile Ile Leu
            195                 200                 205

GAA TAC GAA ATC AAA TAT TTT GAA AAG GAC CAG GAG ACA AGC TAC ACC       670
Glu Tyr Glu Ile Lys Tyr Phe Glu Lys Asp Gln Glu Thr Ser Tyr Thr
        210                 215                 220

ATC ATC AAA TCC AAA GAG ACC GCA ATT ACG GCA GAT GGC TTG AAA CCA       718
Ile Ile Lys Ser Lys Glu Thr Ala Ile Thr Ala Asp Gly Leu Lys Pro
    225                 230                 235
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GGC TCA GCG TAC GTC TTC CAG ATC CGA GCC CGG ACA GCT GCT GGC TAC      766
Gly Ser Ala Tyr Val Phe Gln Ile Arg Ala Arg Thr Ala Ala Gly Tyr
240                 245                 250                 255

GGT GGC TTC AGT CGA AGA TTT GAG TTT GAA ACC AGC CCA GTG TTA GCT      814
Gly Gly Phe Ser Arg Arg Phe Glu Phe Glu Thr Ser Pro Val Leu Ala
                260                 265                 270

GCA TCC AGT GAC CAG AGC CAG ATT CCT ATA ATT GTT GTG TCT GTA ACA      862
Ala Ser Ser Asp Gln Ser Gln Ile Pro Ile Ile Val Val Ser Val Thr
            275                 280                 285

GTG GGA GTT ATT CTG CTG GCT GTT GTT ATC GGT TTC CTT CTC AGT GGA      910
Val Gly Val Ile Leu Leu Ala Val Val Ile Gly Phe Leu Leu Ser Gly
        290                 295                 300

AGG CGC TGT GGC TAC AGC AAG GCT AAA CAA GAC CCA GAA GAA GAA AAG      958
Arg Arg Cys Gly Tyr Ser Lys Ala Lys Gln Asp Pro Glu Glu Glu Lys
    305                 310                 315

ATG CAT TTT CAT AAT GGC CAC ATT AAA CTG CCT GGT GTA AGA ACC TAC     1006
Met His Phe His Asn Gly His Ile Lys Leu Pro Gly Val Arg Thr Tyr
320                 325                 330                 335

ATT GAT CCC CAC ACC TAT GAG GAC CCT AAT CAA GCT GTC CAC GAG TTT     1054
Ile Asp Pro His Thr Tyr Glu Asp Pro Asn Gln Ala Val His Glu Phe
                340                 345                 350

GCC AAG GAA ATA GAA GCT TCG TGC ATA ACC ATC GAG AGA GTT ATC GGA     1102
Ala Lys Glu Ile Glu Ala Ser Cys Ile Thr Ile Glu Arg Val Ile Gly
            355                 360                 365

GCT GGT GAA TTT GGA GAA GTC TGC AGT GGA CGG CTG AAA CTG CAG GGA     1150
Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Gln Gly
        370                 375                 380

AAA CGC GAG TTT CCA GTG GCT ATC AAA ACC CTG AAG GTG GGC TAC ACA     1198
Lys Arg Glu Phe Pro Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr
    385                 390                 395

GAG AAG CAA AGG CGA GAT TTC CTG GGA GAA GCG AGC ATC ATG GGG CAG     1246
Glu Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser Ile Met Gly Gln
400                 405                 410                 415

TTC GAC CAC CCC AAC ATC ATC CAC CTG GAA GGT GTC GTC ACA AAA AGC     1294
Phe Asp His Pro Asn Ile Ile His Leu Glu Gly Val Val Thr Lys Ser
                420                 425                 430

AAA CCT GTA ATG ATA GTA ACG GAA TAC ATG GAA AAT GGT TCT CTG GAT     1342
Lys Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp
            435                 440                 445

ACA TTT TTA AAG AAG AAC GAT GGG CAG TTC ACG GTC ATT CAG CTG GTC     1390
Thr Phe Leu Lys Lys Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val
        450                 455                 460

GGG ATG CTG CGA GGC ATC GCA TCA GGG ATG AAG TAC CTG TCT GAC ATG     1438
Gly Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr Leu Ser Asp Met
    465                 470                 475

GGT TAC GTA CAC AGA GAC CTC GCT GCC AGG AAT ATC CTC ATC AAC AGC     1486
Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Ile Asn Ser
480                 485                 490                 495

AAC TTA GTC TGC AAG GTG TCT GAC TTT GGC CTC TCC AGA GTC CTA GAA     1534
Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu
                500                 505                 510
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GAT GAT CCT GAA GCA GCG TAC ACA ACC AGG GGA GGG AAG ATC CCC ATC      1582
Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile
            515                 520                 525

CGA TGG ACG GCA CCT GAA GCA ATC GCC TTC CGC AAA TTC ACG TCG GCC      1630
Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala
        530                 535                 540

AGC GAT GTG TGG AGC TAC GGC ATT GTG ATG TGG GAA GTG ATG TCC TAT      1678
Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr
    545                 550                 555

GGC GAG AGA CCT TAC TGG GAA ATG ACA AAC CAA GAT GTG ATT AAA GCC      1726
Gly Glu Arg Pro Tyr Trp Glu Met Thr Asn Gln Asp Val Ile Lys Ala
560                 565                 570                 575

GTG GAG GAA GGC TAT CGC CTG CCA AGT CCC ATG GAC TGC CCT GCT GCT      1774
Val Glu Glu Gly Tyr Arg Leu Pro Ser Pro Met Asp Cys Pro Ala Ala
                580                 585                 590

CTC TAC CAG TTG ATG CTT GAC TGC TGG CAG AAA GAC CGC AAC AGC AGG      1822
Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Ser Arg
            595                 600                 605

CCC AAG TTT GAT GAA ATT GTC AGC ATG TTG GAC AAG CTC ATC CGT AAC      1870
Pro Lys Phe Asp Glu Ile Val Ser Met Leu Asp Lys Leu Ile Arg Asn
        610                 615                 620

CCA AGC AGC TTG AAG ACG TTG GTT AAT GCA TCG AGC AGA GTA TCA AAT      1918
Pro Ser Ser Leu Lys Thr Leu Val Asn Ala Ser Ser Arg Val Ser Asn
    625                 630                 635

TTG TTG GTA GAA CAC AGT CCA GTG GGG AGC GGT GCC TAC AGG TCA GTG      1966
Leu Leu Val Glu His Ser Pro Val Gly Ser Gly Ala Tyr Arg Ser Val
640                 645                 650                 655

GGT GAG TGG CTG GAA GCC ATC AAA ATG GGT CGA TAC ACC GAG ATT TTC      2014
Gly Glu Trp Leu Glu Ala Ile Lys Met Gly Arg Tyr Thr Glu Ile Phe
                660                 665                 670

ATG GAG AAT GGA TAC AGT TCG ATG GAT TCT GTG GCT CAG GTG ACC CTA      2062
Met Glu Asn Gly Tyr Ser Ser Met Asp Ser Val Ala Gln Val Thr Leu
            675                 680                 685

GAG GAC GAA TCA CCT TGT GAA AAG TGG AGC CTC ACC CTC CAC CCC CTC      2110
Glu Asp Glu Ser Pro Cys Glu Lys Trp Ser Leu Thr Leu His Pro Leu
        690                 695                 700

TTT CCA ACT GGA TAT CAG ACT TGAAGGAAAC CTTTCCAGTG GACCAGACCT         2161
Phe Pro Thr Gly Tyr Gln Thr
    705                 710

GCTCTTTAAA CTTGTGGACC ACCTAGTGAC TTTGAGTGTG TCTGGAGCTC TTTCAATCCA    2221

CTGCAAGAAT AACTTTACCA GGACAGTACT CAAGAATAGA TAGATCCATG ACATGAGTTT    2281

CAGTCTGATA TTTGACTGGA CCAATTACTA ACAAAATGTG GACTGCATAC TTACACCTTT    2341

TGAAAGATCT GTACTCACCG AATCTCAGGA CACCCTGTTG TTTGTTATTA GATGAAGAAC    2401

TCTGAATATT TGTAATAATA TGTGATGTGT TGCTTTGCAT TGTATTTTTT TCTTATAAAA    2461

TAAAATAAAT TATTTATTAA AAGTTATACT GGGATGAAGA CCATTTAAGA GTTCACCTGC    2521

TCTAGATGCT TATTCTTAAC CTGAAACCTC AGTTCCGGAT AGTGATACTG CACACGCTTG    2581

TGAACAAACC CATTCTCGTG TCATAACCAA ACAGGATGGG AGTAATGAAT AAGAGCAGAT    2641
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GAACTCTTAA AAGAAAGATC CTAATCTCAT GCAAAGGTCC CTTGCAAGTG GATTCCTCTC 2701

TCCCTAGCGT CTTCTAAAGG TCTTTGAGGT TATTCTTTCC CCTCTTTCAA ACTGACAGCT 2761

AACTCTGTGA GTAGTGTCAG TCTGCATGGG CCAGTGTAGA ACTGCACCAT GTTGAAGAAG 2821

AGTGCTGCAA TATGGCTGGG GTGGGAGATG AAATGCAAAG TAATCTCTGG TAGGCTGATG 2881

GCTTCCAGCC ATGGAGGTAT TTCAGGAACC TGGCCCTTTT GCTTGCATGA GTAATGAATG 2941

GAGTGGTGAG GAGTGTTGTA TTTTATGTGG CAATCCAGTC CTAGTCTACA CTGTGTTTGA 3001

CAAATTGGTC CATGGTGTAT AAGTAGTTCT ATTTGTAAAT AAAATGTTTT AAATG 3056

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 710 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu Gly
1 5 10 15

Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp Glu
20 25 30

Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr Ile
35 40 45

Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val Met
50 55 60

Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys Gly
65 70 75 80

Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val Ser
85 90 95

Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu Ala
100 105 110

Arg Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu Glu
115 120 125

Val Ser Gly Val Cys Val Asn His Ser Val Thr Asp Glu Ala Pro Lys
130 135 140

Met His Cys Ser Ser Glu Gly Glu Trp Leu Val Pro Ile Gly Lys Cys
145 150 155 160

Leu Cys Lys Ala Gly Tyr Glu Glu Lys Asn Asn Thr Cys Gln Ala Pro
165 170 175

Ser Pro Val Ser Ser Val Lys Lys Gly Lys Ile Thr Lys Asn Ser Ile
180 185 190

Ser Leu Ser Trp Gln Glu Pro Asp Arg Pro Asn Gly Ile Ile Leu Glu
195 200 205

Tyr Glu Ile Lys Tyr Phe Glu Lys Asp Gln Glu Thr Ser Tyr Thr Ile
210 215 220

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Ile Lys Ser Lys Glu Thr Ala Ile Thr Ala Asp Gly Leu Lys Pro Gly
225                 230                 235                 240

Ser Ala Tyr Val Phe Gln Ile Arg Ala Arg Thr Ala Ala Gly Tyr Gly
                245                 250                 255

Gly Phe Ser Arg Arg Phe Glu Phe Glu Thr Ser Pro Val Leu Ala Ala
            260                 265                 270

Ser Ser Asp Gln Ser Gln Ile Pro Ile Ile Val Val Ser Val Thr Val
        275                 280                 285

Gly Val Ile Leu Leu Ala Val Val Ile Gly Phe Leu Leu Ser Gly Arg
    290                 295                 300

Arg Cys Gly Tyr Ser Lys Ala Lys Gln Asp Pro Glu Glu Glu Lys Met
305                 310                 315                 320

His Phe His Asn Gly His Ile Lys Leu Pro Gly Val Arg Thr Tyr Ile
                325                 330                 335

Asp Pro His Thr Tyr Glu Asp Pro Asn Gln Ala Val His Glu Phe Ala
            340                 345                 350

Lys Glu Ile Glu Ala Ser Cys Ile Thr Ile Glu Arg Val Ile Gly Ala
        355                 360                 365

Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Gln Gly Lys
    370                 375                 380

Arg Glu Phe Pro Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr Glu
385                 390                 395                 400

Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser Ile Met Gly Gln Phe
                405                 410                 415

Asp His Pro Asn Ile Ile His Leu Glu Gly Val Val Thr Lys Ser Lys
            420                 425                 430

Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Thr
        435                 440                 445

Phe Leu Lys Lys Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly
    450                 455                 460

Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr Leu Ser Asp Met Gly
465                 470                 475                 480

Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Ile Asn Ser Asn
                485                 490                 495

Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu Asp
            500                 505                 510

Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg
        515                 520                 525

Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala Ser
    530                 535                 540

Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly
545                 550                 555                 560

Glu Arg Pro Tyr Trp Glu Met Thr Asn Gln Asp Val Ile Lys Ala Val
                565                 570                 575
```

```
Glu Glu Gly Tyr Arg Leu Pro Ser Pro Met Asp Cys Pro Ala Ala Leu
           580                 585                 590

Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Ser Arg Pro
       595                 600                 605

Lys Phe Asp Glu Ile Val Ser Met Leu Asp Lys Leu Ile Arg Asn Pro
   610                 615                 620

Ser Ser Leu Lys Thr Leu Val Asn Ala Ser Ser Arg Val Ser Asn Leu
625                 630                 635                 640

Leu Val Glu His Ser Pro Val Gly Ser Gly Ala Tyr Arg Ser Val Gly
               645                 650                 655

Glu Trp Leu Glu Ala Ile Lys Met Gly Arg Tyr Thr Glu Ile Phe Met
           660                 665                 670

Glu Asn Gly Tyr Ser Ser Met Asp Ser Val Ala Gln Val Thr Leu Glu
       675                 680                 685

Asp Glu Ser Pro Cys Glu Lys Trp Ser Leu Thr Leu His Pro Leu Phe
   690                 695                 700

Pro Thr Gly Tyr Gln Thr
705                 710
```

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

```
Arg Ile Cys Thr Pro Asp Val Ser Gly Thr Val Gly Ser Arg Pro Ala
1               5                   10                  15

Ala Asp His
```

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 13 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

```
Cys Leu Glu Thr His Thr Lys Asn Ser Pro Val Pro Val
1               5                   10
```

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Lys Met Gln Gln Met His Gly Arg Met Val Pro Val
1 5 10

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Lys Val His Leu Asn Gln Leu Glu Pro Val Glu Val
1 5 10

What is claimed is:

1. A composition of matter, comprising an isolated nucleic acid sequence encoding a Eph-related protein tyrosine kinase, or functional fragment thereof, having about 23 to 66 percent amino acid sequence identity in its carboxyl terminal variable region compared to known members of the Eph subclass of tyrosine kinases.

2. The composition of claim 1, comprising substantially the same nucleotide sequence selected from the group consisting of SEQ ID NOS: 3, 7, 9, 11, 13, 19 and 21.

3. A composition of matter, comprising a vector containing the nucleic acid of claim 1.

4. The composition of claim 3, wherein said vector is for the expression of a recombinant Eph-related protein tyrosine kinase.

5. The composition of claim 4, wherein said expression is in a procaryotic host.

6. The composition of claim 4, wherein said expression is in a eucaryotic host.

7. A composition of matter, comprising a host cell containing the vector of claim 3.

8. The composition of claim 7, wherein said host cell is procaryotic.

9. The composition of claim 7, wherein said host cell is eucaryotic.

10. A composition of matter, comprising a substantially purified Eph-related protein tyrosine kinase, or functional fragment thereof, having about 23 to 66 percent amino acid sequence identity in its carboxyl terminal variable region compared to known members of the Eph subclass of tyrosine kinases.

11. The composition of claim 10, comprising substantially the same amino acid sequence selected from the group consisting of SEQ ID NOS: 4, 8, 10, 12, 14, 20 and 22.

12. A composition of matter, comprising a substantially purified chicken Eph-related protein tyrosine kinase, or functional fragment thereof having substantially the same amino acid sequence of SEQ ID NO: 2.

13. A composition of matter, comprising a substantially purified chicken Eph-related protein tyrosine kinase, or functional fragment thereof having substantially the same amino acid sequence of SEQ ID NO: 6.

14. A method of diagnosing cancer, comprising removing a tissue or cell sample from a subject suspected of having cancer and determining the level of Eph-related protein tyrosine kinase in said sample, wherein a change in the level or activity of a Eph-related protein tyrosine kinase compared to a normal sample indicates the presence of a cancer or correlates with a specific prognosis.

15. The method of claim 13, wherein an increase in said change in the level or activity of a Eph-related protein tyrosine kinase indicates the presence of a cancer or correlates with a specific prognosis.

16. The method of claim 13, wherein a decrease in said change in the level or activity of a Eph-related protein tyrosine kinase indicates the presence of a cancer or correlates with a specific prognosis.

17. The method of claim 12, wherein said cancer is selected from the group consisting of liver carcinoma, lung carcinoma, breast carcinoma, colon carcinoma and leukemia.

```
Cek5     1   MPGPERTMGPLWFCCLPLALLPLLAAVEETLMDSTTATAELGWMVHP-PSGWEEVSGYDENMNTIRTYQVCNVFE-SSQNNWLRTKYIRRR-GAHRIH
Cek10    1                    GVSSRARRPPGSSRSSRRGV.S..A.TT..-ET.........A.QP.......Q.R.-AQ.QQ.....F.N.Q-DVQ.VY
Cek6     1                          .....TR.........TAN.-;.............L.............-PN.....L.TF.N..-.....Y
Cek4     1   .DRRRLPLLL.CAALGSAGR.SARPGN.VN.L..K.IQG....ISY.-SH....I..V..HYTP.....ES..MD-H.........NW.P.N-S.QK.Y
EcK      1  MELQAARACFAL..G.--A..AAAAAQGK.VV.L.FAA.GG....LT..YGK..DLMQNIMND.-P.YM.S....MS-GD.D.....NWVY.G-E.E.NN
Eph      1  MERRW.LGLGLV.LL.---AP.P.GAR.K.V....TSK.QG....LLD.PKD..S.QQQILNGT-PLYM..D.PMQGRRDTDH...SNW.Y.GEE.S.V.

Cek5    96  VEMKFSVRDCSSIPNVPG--SCKETFNLYYYESDFDSATKTFPNWMENPWMKVDTIAADESFSQVDLGGRVMKINTEVRSFGPVSKNGFYLAFQDYGGCM
Cek10   79  ..L..T....K...KI..--........F.....T...SANS.F.....YI......P.....KLES.-..---..K......L...........L.A..
CeK6    68  T..R.T......L.....--............T.SVI...KSAF.T.A.YL..............F...L..GF----------------------
Cek8     1                                        GESQ---FA.I.........T...I.D.I..L.....DV..L..K........V.A.I
Cek4    96  ..L..TL...N...L.L.--T.........M...D.HLA.-.REHQ---FT.I.........T.M...D.IL.L.....EV.....K........V.A.V
Eck     96  F.LN.T....N.F.GGAS--..........A...L.YG.N-.QKRL---FT.I....P..ITVSS.FEA.HV.L.V.E..V..LTRK........I.A.V
Eph     97  ..LQ.T....K.F.GGA.PLG.......L.M...Q.VGIQ-LRRPL---FQ..T.V...Q..TIR..ASGSV.L.V.RC.L.RLTRR.L....HNP.A.V

Cek5   194  SLIAVRVFYRKCPRVIQNGAVFQETLSGAESTSLVAARGTCISNA---EEVDVPIKLYCNGDGEWLVPIGRCMCRPGYESVENGTVCRGCPSGTFKASQG
Cek10  173  ...L..A..K..SNT.AGF.I.P...T...P....I.P....PQ.---V..S..L..........M..V.A.T.AA...PAMKD.Q.QA.GP....SK..
Cek6   141  --------.FK...S.V..F.I.P..MT........T......P..---.................M......T.KA...PEN.-VA..A..A........
Cek8    56  A.VS.....K...LTVR.L.Q.PD.IT..DTS...EV..S.VN.S---..K...-.M..GA.........N.L.NA...ERNG--E.QA.KI.YY..LST
Cek4   190  A.VS...YFK...FTVK.L.M.PD.VPM-D.Q...EV..S.VNHS---K.EEP.-.M..STE........K.L.NA...ERGF--A.QA.RP.FY...A.
Eck    190  A.LS...Y.K...ELL.GL.H.P..IA.SDAP..ATVA...VDH.VVPPGGEE.-RMH.AV.........Q.L.QA...K..D--A.QA.SP.F..FEAS
Eph    193  A.VS.....QR..ETLNGL.Q.PD..P.--PAG..EVA...LPH.RASPRPSGAPRMH.SP... ...V...H.E....EGGS.EA.VA....SYRMDMD
```

FIG. IA

```
                 " "          " "          " o          o o o o   o    o o " "       " "
Cek5   291  DEGCVHCPINSRTTSEGATNCVCRNGYYRADADPVDMPCTTIPSAPQAVISSVNETSLMLEWTPPRDSGGREDLVYNIICKSCGS---GRGACTRCGDNV
Cek10  270  EGP.SP..P.....AGA..V.I..S.FF......A.SA..SV....RS...N.....FV...SE.Q.A...D..L..V...K.SV---E.RL.S..D...
Cek6   230  AGL.AR..P...SSA.ASPL.A.....F...L..PTAA..SV..G.RN...I.....II...N...ET...D.VT...V..K.RA---D.R..S..D...
Cek9     1                                                                                                V......
Cek8   150  .VA.AK..PH.YSIW..S.S.T.DR.FF..EN.AAS....RP.....NL..N.....VN...SA.QNK...D.IS..VV..R..A---.EPSH.RS..SG.
Cek4   283  NVK.AK..PH.S.YEDASLN.R.EKN.F.SEK..PS.A..RP....RN...NI....VI.D.SW.L.T...K.VTF.....K..G---SSKI.EP.S...
Eck    287  ESP.LE..EHTLPSP....S.E.EE.FF..PQ..AS....RP....HYLTAVGMGAKVE.R....Q.......I..SVT.EQ.WP---ES.E.GP.EAS.
Eph    291  TPH.LT..QQ.TAE.....I.T.ES.H...PGEGPQVA..GP....RNLSF.ASG.Q.S.R.E..A.T...Q.VR.SVR.SQ.QGTAQDG.P.QP..VG.

                          o o     o   o o                    *                  * * * *    *    * *
Cek5   388  QFAPRQLGLTEPRIYISDLLAHTQYTFEIQAVNGVTDQSPFSPQFASVNITTNQAAPSAVSIMHQVSRTVDSITLSWSQPDQPNGVILDYELQYYEKNL-
Cek10  367  E.V........R.....KVM..P...........ISSK..YP.H...........VL...PT..LH.S.GN.M....TP.ER...I.....IK.S..QGQ
Cek6   327  E.V........T.VF..S.W...P...........SNK...P..HV...........T.P......A.MR......P..E....I......R....LS+
Cek9     8  ..E...V....S.VQV.N...RV..........L..EL.SEA..Y.TI.VS.S.SV...IPM......ATS......P...........Q.R.FD.AE-
Cek8   248  H.S.Q.N..KTTKVS.T......N....VW.....SKHN.SQD.AV..TV........PIALIQAKEI.RH.VA.A.LE..R......E..VK....DQ-
Cek4   380  R.L...T...NTTVTVV......N.....D.....S.L.TL.R...A.S.........PITVIRKDRTSRN.VS...QE.EH...I.....VK....QE-
Eck    384  RYSEPPH...RTSVTV...EP.MN...TVE.R...SGLVT-.RS.RTASVSI..TE.PK.RL---EGRSTT.LSV...I.PPQQSRVWKELVT.RKNGD-
Eph    391  H.S.GARA..T.AVHVNG.EPYAN...NVE.Q...SGLGSSGHAST..S.SMGH.ESLSGLSLRL.KKEPRQLE.T.AGSRPRSP.AN.T...HVLNQD-

                          * *     *   * *
Cek5   487  SELNSTAVKSPTNTVTVQNLKAGTIYVFQVRARTVAGYGRYSGKMYFQTMTEAEYQTSVQEKLPLIIGSSAAGLVFLIAVVVIIIVCN----------
Cek10  467  GDGIANT.T.QK.S.RLDG...NAR.MV.............LPTE...TA.DGSTSKTFQE...V..AT...L.V.V..I.A...F-----(RKGMVT
Cek6   445  N.Y..SVAR.Q...ARLEG.RP.MV..V...........K.....C...L.DDD.KSELR.Q...A..A...V..IVSL.A.S...S----------
Cek9   107  D.D..FTLT.E..MA.IL..SP.K..........AV...P.........LMGG.HSEMA.DR...V..ALG..A..VIAAIA.LAII----------
Cek8   347  N.RTYRI..TASRNTDIKG.NPL.S...H.....A....DF..PFE.T.N.VPSP-IIGDGTN.TVLLV.V..S.V.VVILIAAF.IS----------
Cek7     1                          ....I....A....GF.RRFE.E.SPVLAA-S.D.SQI.I.VV.VTV.VIL.AV.IGELLSGSCCDHGCGWASSL
Cek4   479  Q.TSY.ILRAKSTN..ISG..PD.T....I....A.R..TS.R.FE.E.SPDSFSIS.ENSQVVM.AI.A.VAIIL.TV..YVL.G----------
Eck    479  -SNSYNVRRTEGFS..LDD.APD.T.LV..Q.L.QE.Q.AG.KVHE...LS------PEGSGNIAV..GV.V.V.I.LVLAGVGFFIH----------
Eph    491  ----ERYQMVLEPR.LLTE.QPD.T.IVR..ML.PL.P.PF.PDHE.R.SPPVSR-GLTGGEIVAV.FGLLL.AAL.LGIL.FRSRRA----------
```

FIG. 1B

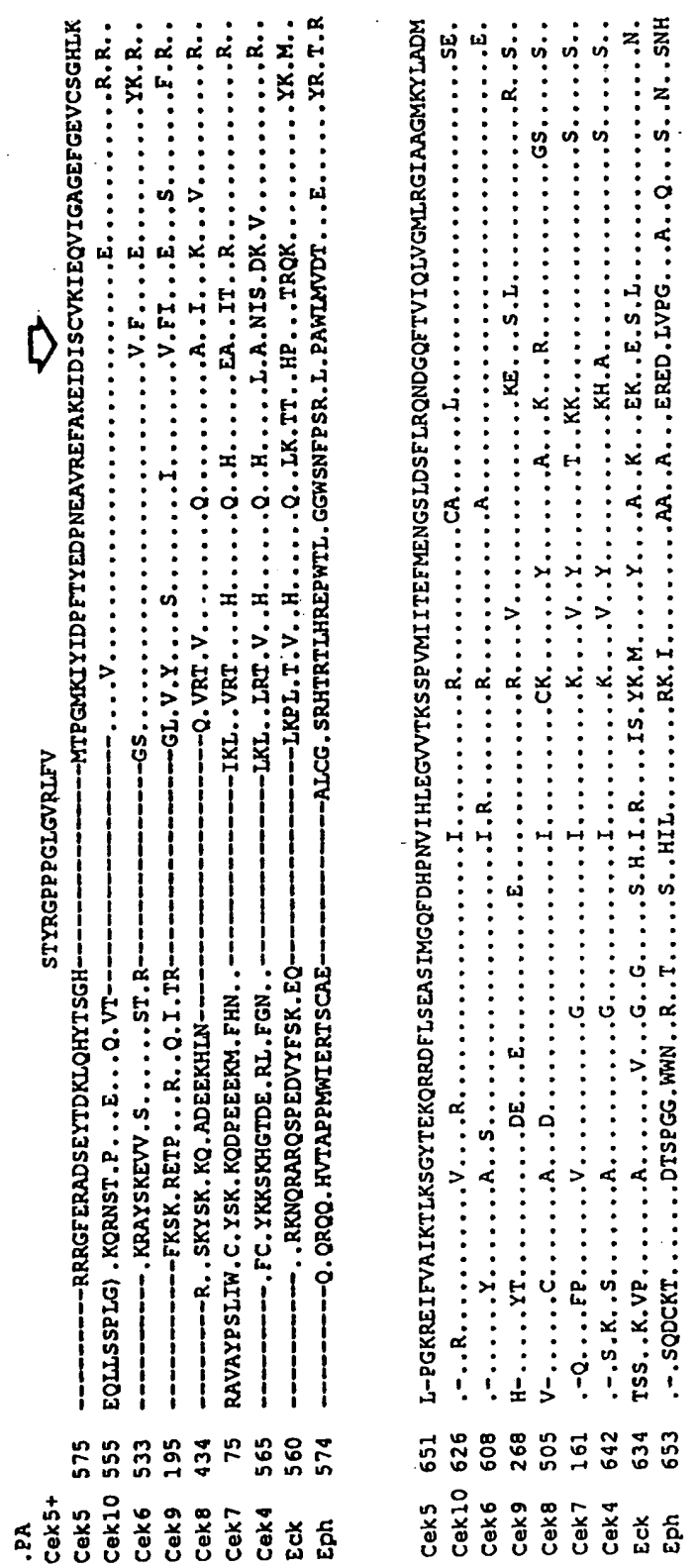

.PA
STYRGPPPGLGVRLFV
Cek5+
Cek5 575 ----------RRRGFERADSEYTDKLQHYTSGH----------MTPGMKIYIDPFTYEDPNEAVREFAKEIDISCVKIEQVIGAGEFGEVCSGHLK
Cek10 555 EQLLSSPLG).KQRNST.P...E...Q.VT----------.....V.....E.....R.R..
Cek6 533 ----------.KRAYSKEVV.S.....ST.R----------GS.....V.F....E.....YK.R..
Cek9 195 ----------FKSK.RETP...R..Q.I.TR----------GL.V.Y....S.....I.....V.FI...E...S.....F.R..
Cek8 434 ----------R..SKYSK.KQ.ADEEKHLN----------Q.VRT.V.....Q.....A.I...K...V.....R..
Cek7 75 RAVAYPSLIW.C.YSK.KQDPEEERM.FHN.----------IKL..VRT....H.....Q..H.....EA..IT..R.....R..
Cek4 565 ----------.FC.YKKSKHGTDE.RL.FGN.----------LKL..LRT.V..H.....Q..H.....L.A.NIS.DK.V.....R..
Eck 560 ----------..RKNQRARQSPEDVYFSK.EQ----------LKPL.T.V..H.....Q..LK.TT..HP...TRQK.....YK.M..
Eph 574 ----------Q.QRQQ.HVTAPPMWIERTSCAE----------ALCG.SRHTRTLHREPWTL.GGWSNFPSR.L.PAWLMVDT...E.....YR.T.R
Cek5 651 L-PGKREIFVAIKTLKSGYTEKQRRDFLSEASIMGQFDHPNVIHLEGVVTKSSPVMIITEFMENGSLDSFLRQNDGQFTVIQLVGMLRGIAAGMKYLADM
Cek10 626 .-..R.....V....R.....I.....R.....CA.....L.....SE.
Cek6 608 .-.....Y.....A..S.....I.R.....R.....A.....E.
Cek9 268 H-.....YT.....DE...E.....E.....R....V.....KE...S.L.....R..S..
Cek8 505 V-.....C.....A....D.....I.....CK.....Y.....A...K...R.....GS.....S..
Cek7 161 .-Q.....FP.....V.....I.....K....V..Y.....T..KK.....S.....S..
Cek4 642 .-.S.K..S.....A.....G.....I.....K....V..Y.....KH.A.....S.....S..
Eck 634 TSS..K.VP.....A.....V...G..G.....S.H.I.R....IS.YK.M.....Y....A..K...EK..E.S.L.....N.
Eph 653 .-.SQDCKT.....DTSPGG.WWN..R..T.....S..HIL.....RK.I.....AA..A...ERED.LVPG...A..Q...S..N..SNH

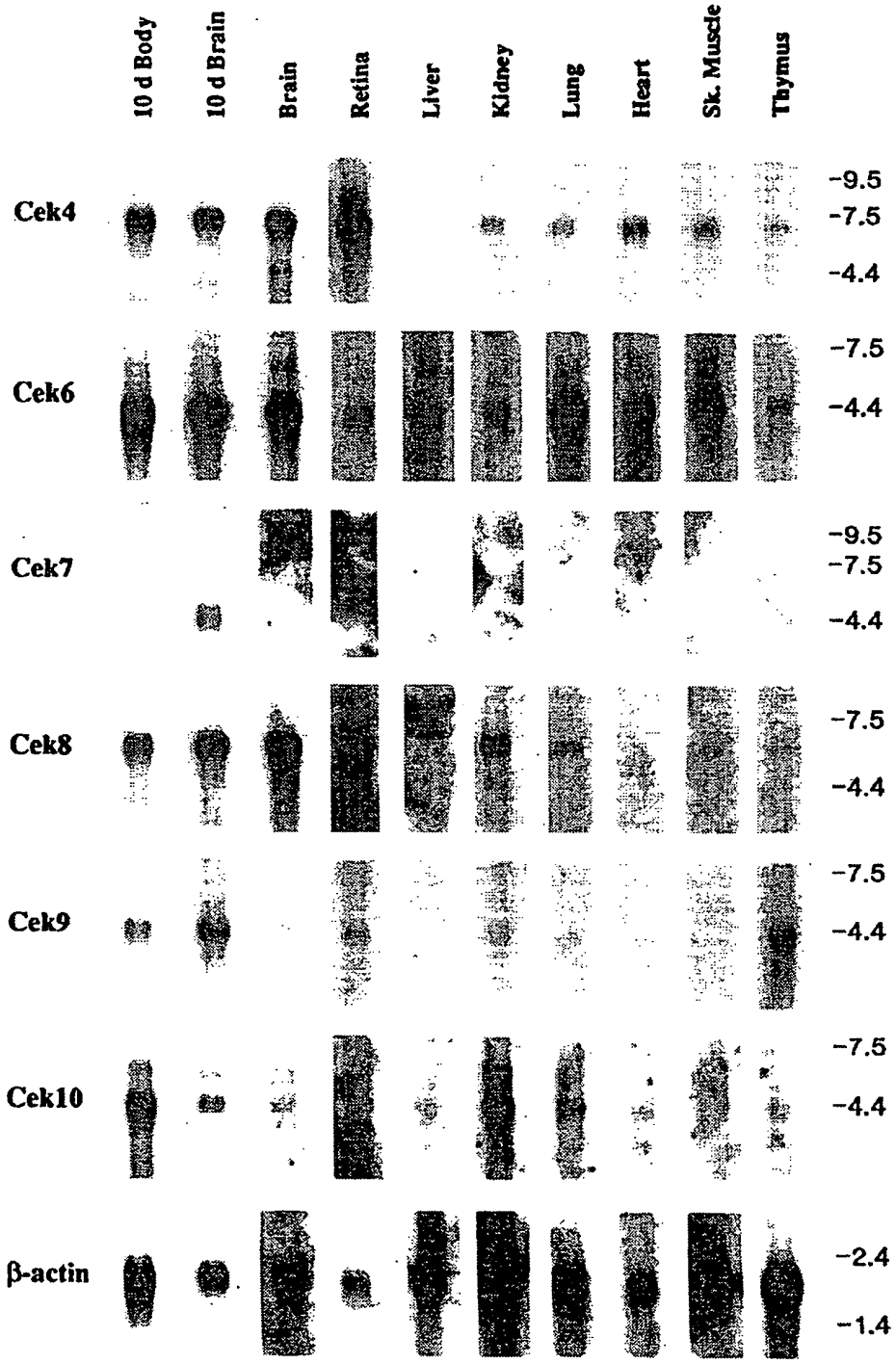
FIG. IC

```
Cek5   750  NYVHRDLAARNILVNSNLVCKVSDFGLSRFLEDDTSDPTYTSALGGKIPIRWTAPEAIQYRKFTSASDVWSYGIVMWEVMSYGERPYWDMTNQDVINAIE
Cek10  725  ................................PA......S.............A.............................S.......V.
Cek6   707  ............................Y.Q.........S......V........A.....................F........S.........
Cek9   367  ................................A.N....G...C...........V.......S.....................S........D
Cek8   604  S.........................M..V....-PEAA..TR-.............A.............................S.....K...
Cek7   260  G............I.............V....-PEAA..TR-.............AF............................E.......K.V.
Cek4   741  G............I.............V....-PEAA..TR-.........S....A.........A......L............E.SF....K.VD
Eck    734  ............................V....-PEA...TS-.............S............F.........T.......ELS.HE.MK..N
Eph    752  ..............Q..C........T.L.D.--F.G..ETQ-.............AH.I..T......F.......L.F.DK..GE.S..E.MKS..

Cek5   850  QDYRLPPPMDCPNALHQLMLDCWQKDRNHRPKFGQIVNTLDKMIRNPNSLKAMAPLSSGVNLPLLDRTIPDYTSFNTVDEWLDAIKMSQYKESFASAGFT
Cek10  825  ............T..........VR...L....A.........L...AA...VI.SVQ...SQ......V....T.T..GD.......GR...N.VN...A
Cek6   807  ............A..............T..RLAE............A...TV.TITAVPSQ.....S...F.A.TS.ED..S.V.....RDN.L.....
Cek9   467  .........P...TV..L..........VQ....E...SA......K.SA...TGTG..RPSQ...SNSP..FP.LSNAH........GR...N.DQ..LI
Cek8   702  EG..........I............E.SD.........M...L........RTGSE..RPSTA...PSS.EFSAVVS.SD..Q....ER..DN.TA..Y.
Cek7   358  EG....S.....A..Y............S....DE..SM...L....S...TLVNA..R.SNL.VEHSPVGSGAYRS.G...E....GR.T.I.MEN.YS
Cek4   839  EG..........A..Y............N....E...SI...L....S...IITNAAARPSNL...QSNI.ISA.R.AGD..NGFRTG.C.GI.TGVEYS
Eck    832  DGF...T.....S.IY...MQ...QE.AR....AD..SI...L..A.D...TL.DFDPR.SIR.PSTSGSEGVP.R..S...ES...Q..T.H.MA..Y.
Eph    849  DG......V...AP.YE..KN..AY..AR..H.QKLQAH.EQLLA..H..RTI.NFDPR.T.R.PSLSGS.GIPYR..S...ES.R.KR.ILH.H...LD

Cek5   950  TFDIVSQMTVEDILRVGVTLAGHQKKILNSIQVMRAQMNQIQSVEV
Cek10  924  S..L.A...A..L..I............S...D..L....TLP.Q.
Cek6   907  SLQL.A...S..L..I................S..V..S.SPTSMA
Cek9   567  ...VI.R..L..LQ.I.I..V...........L.KVHL..LEP...
Cek8   802  .LEA.VH.NQD.LA.I.I.AIT..N...S.V.A..S..Q.MHGRM.PV
Cek7   458  SM.S.A.V.L..---------ESPCE.WSLTLHPLFPTGY.T
Cek4   939  SC.TIAKISTD.MKK....VV.P....VS..KTLETHTKNSPVPV
Eck    932  AIEK.V...ND..K.I..R.P....R.AY.LLGLKD.V.TVGIPI
Eph    949  .MEC.LEL.A..LTQM.I..P....R..C...GFKD
```

FIG. ID


10 d Body
10 d Brain
Brain
Retina
Liver
Kidney
Lung
Heart
Sk. Muscle
Thymus
Cek4
Cek6
Cek7
Cek8
Cek9
Cek10
β-actin
-9.5
-7.5
-4.4
-7.5
-4.4
-9.5
-7.5
-4.4
-7.5
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-4.4
-2.4
-1.4

FIG. 2

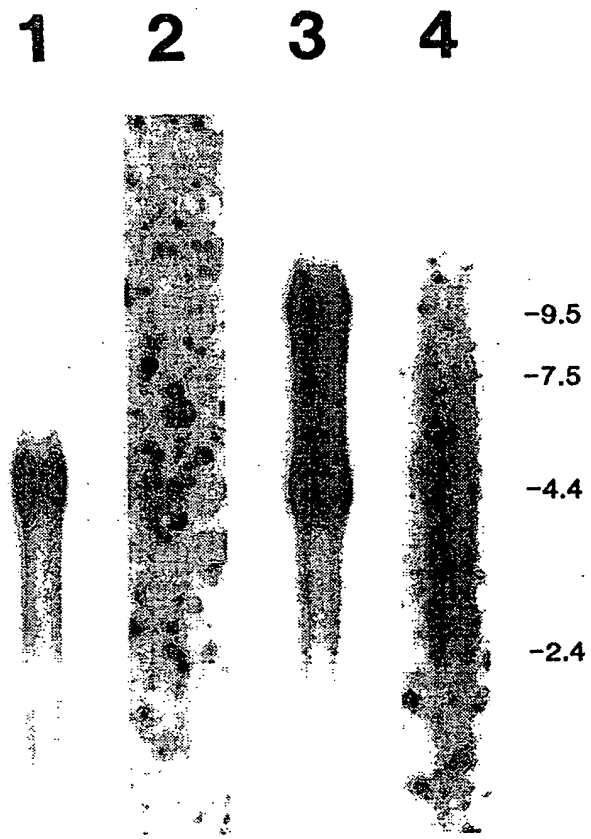


FIG. 3

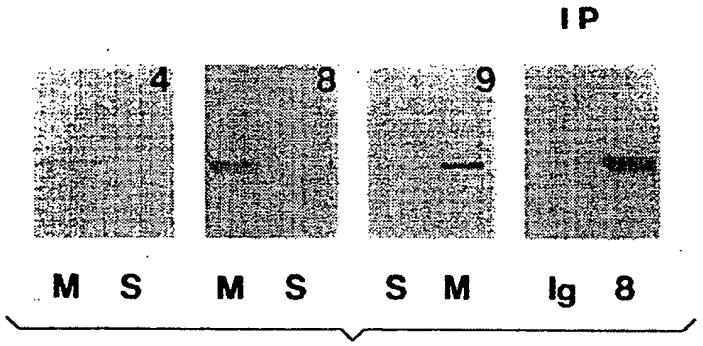


FIG. 4

FIG. 5A

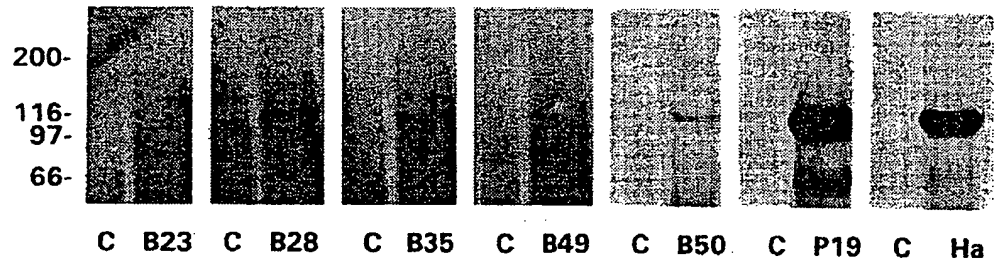


FIG. 5B

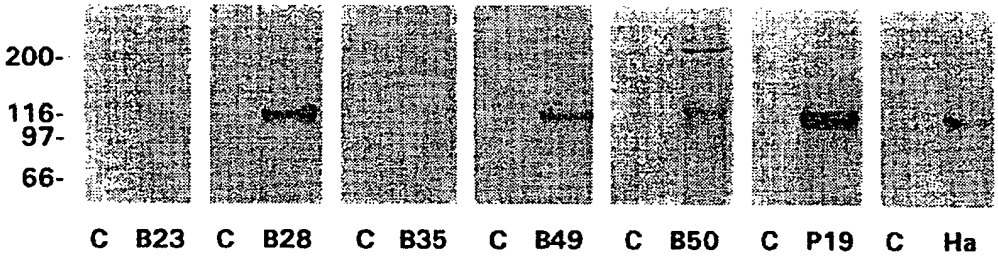


FIG. 5C

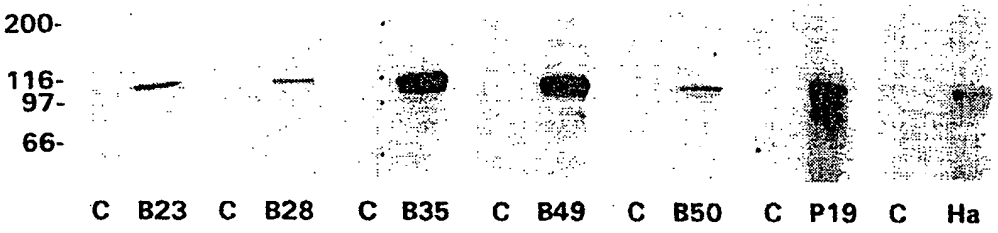


FIG. 5D

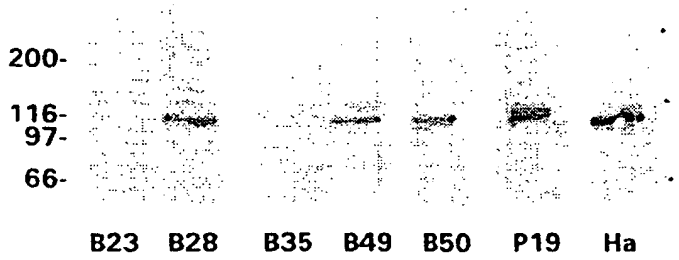
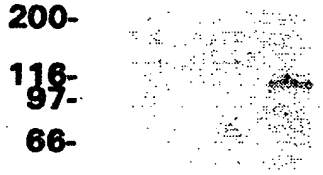
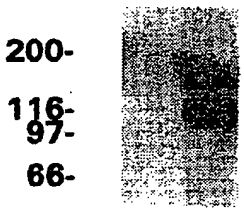


FIG.6A



10d Ad LMH

FIG.6C



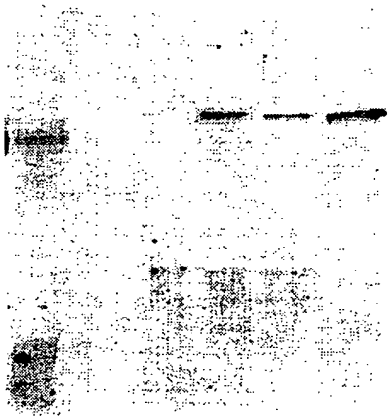
CEF RSV

FIG.6D

CEF RSV

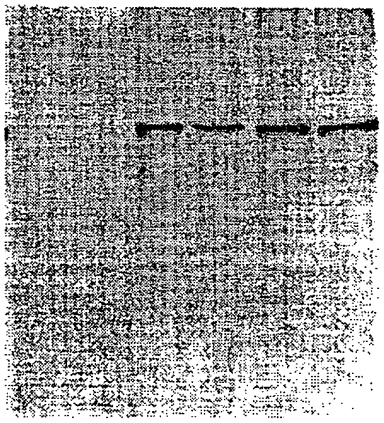
FIG.6B

FIG.6E



1 2 3 4 5

FIG.6F



1 2 3 4 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/10140

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C12N 15/00, 9/00
US CL :435/240.2, 252.3, 320.1, 194; 536/23.2, 23.5
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/240.2, 252.3, 320.1, 194; 536/23.2, 23.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Dialog, APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Oncogene, Volume 320, issued 1992, Gilardi-Hebenstreit et al., "An Eph-related receptor protein tyrosine kinase gene segmentally expressed in the developing mouse hindbrain", pages 2499-2507, see entire document.	1-9
Y	Cell Regulation, Volume 2, issued July 1991, E. B. Pasquale, "Identification of chicken embryo kinase 5, a developmentally regulated receptor-type tyrosine kinase of the Eph family", pages 523-534, see entire document.	1-9

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 22 NOVEMBER 1994	Date of mailing of the international search report 10 JAN 1995
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer KEITH D. HENDRICKS Telephone No. (703) 308-0196

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/10140

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Proceedings of the National Academy of Sciences USA, Volume 89, issued March 1992, Wicks et al., "Molecular cloning of HEK, the gene encoding a receptor tyrosine kinase expressed by human lymphoid tumor cell lines", pages 1611-1615, see entire document.	1-9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/10140

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

I. Claims 1-9 drawn to the DNA, vector, host cell and method of making protein.
II. Claims 10-13, drawn to the enzyme.
III. Claims 14-17, drawn to a method of using the enzyme of Group II.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The DNA Group I and the protein of Group II are not chemically related, and they are independent and distinct inventive concepts. The DNA possesses utility other than encoding the protein, such as in a hybridization assay or as a probe. The DNA of Group I is not related to the method of Group III for similar reasons, as the method of Group III does not involve the DNA.
Groups II and III are related as a second product and method of use. The method may be used with a materially different enzyme, such as one from another source.

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